I. PATENT ABSTRACTS OF JAPAN

(11)Publication number : **2003-284931**
(43)Date of publication of application : **07.10.2003**

(51)Int.Cl. **B01D 69/08**
A61M 1/18
F26B 3/347
F26B 25/00

(21)Application number : **2002-087779**
(22)Date of filing : **27.03.2002**

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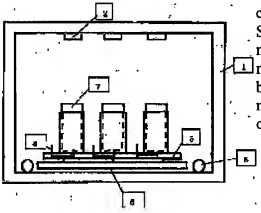
(54) APPARATUS FOR DRYING HOLLOW FIBER MEMBRANE

(57)Abstract:
PROBLEM TO BE SOLVED: To provide an apparatus for drying a wet membrane formed of a plurality of fiber bundles at a time by means of micro-wave irradiation, capable of uniformly drying all the bundles.
SOLUTION: This apparatus for drying the hollow fiber membrane is characterized by comprising, in a vessel a means of micro-wave irradiation, a means to carry the bundles fixed thereon into or out of the vessel, and a means to pass a liquid having a dielectric loss coefficient of 1 to 50 therethrough.



LEGAL STATUS

[Date of request for examination]	13.01.2005
[Date of sending the examiner's decision of rejection]	
[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]	
[Date of final disposal for application]	
[Patent number]	
[Date of registration]	
[Number of appeal against examiner's decision of rejection]	
[Date of requesting appeal against examiner's decision of rejection]	
[Date of extinction of right]	

CLAIMS

[Claim(s)]
[Claim 1] The dryer of the hollow fiber characterized by having a means to pass the liquid whose dielectric loss multipliers are 1-50 the means which is equipment for drying the humid film ****(ed) in the shape of a thread, fixes in a container a microwave exposure means and the humid film ****(ed) in the shape of a thread, and is carried in and taken out, and into a container.
[Claim 2] Equipment according to claim 1 characterized by having piping for passing the liquid whose dielectric loss multipliers are 1-50 around the metal part in a container, or a metal part.
[Claim 3] Equipment according to claim 1 or 2 characterized by two or more microwave exposure means existing.
[Claim 4] Equipment according to claim 1 to 3 characterized by having a means to ventilate to a thread.
[Claim 5] Equipment according to claim 1 to 4 characterized by having further a means to rotate a means to fix, and to carry in and take out the humid film ****(ed) in the shape of a thread.
[Claim 6] Equipment according to claim 1 to 5 characterized by a container having a microwave cutoff function.
[Claim 7] Equipment according to claim 1 to 6 characterized by having further the temperature control means which keeps the temperature in a container constant.
[Claim 8] Equipment according to claim 1 to 7 characterized by having further a means to circulate through the gas in a container.
[Claim 9] Equipment according to claim 1 to 8 characterized by having further a means to permute the gas in a container by the external gas.
[Claim 10] Equipment according to claim 1 to 9 whose hollow fiber is hollow filament-like blood purification film.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention relates to the dryer of a hollow fiber. More, this invention is equipment for drying the humid film ****(ed) in the shape of a thread by microwave exposure at two or more bundle coincidence, and relates to the dryer aiming at preventing the poor engine performance of some [by the local temperature rise in an irradiation reactor] threads, and drying all threads to homogeneity at a detail.

[0002]
[Description of the Prior Art] The technique of using the film which has alternative permeability progresses splendidly in recent years, and utilization in extensive fields, such as a separation filter of a gas or a liquid, hemodialyzer in the medical field, a blood filter, and a constituent-of-blood selection separation filter, is progressing until now. As an ingredient of this film, polymers, such as cellulose types (a regenerated-cellulose system, a cellulose acetate system, chemistry denaturation cellulose type, etc.), a polyacrylonitrile system, a polymethylmethacrylate system, a polysulfone system, a polyethylene vinyl alcohol system, and a polyamide system, have been used. Among these, since haemocompatibility of a polysulfone system polymer improves by in addition to the thermal stability, acid-proof, and alkali resistance adding a hydrophilization agent to a film production undiluted solution, and producing a film to it, it was observed as a semipermeable membrane raw material, and research has been advanced.
[0003] On the other hand, in order to paste up the film and to produce a module, it is necessary to dry the film but, and if the porous membrane which consists of an organic macromolecule, the permeable membrane which consists of hydrophobic polymers, such as a polysulfone system, especially, and ultrafiltration membrane are dried after film production, it is known that the amount of water penetration will fall remarkably compared with desiccation before. Therefore, the film always needed to be dealt with in the damp or wet condition and the condition of having made water immersed.
[0004] The approach taken from the former as this cure was putting low volatility organic liquids, such as a glycerol, in the hole part in porous membrane after film production and before desiccation. However, since hyperviscosity [a low volatility organic liquid] generally, although washing clearance took time amount, module molding of the film was carried out and after washing was a minute amount, the problem was to see the effluent of the low volatility organic liquid origin etc. in module mounting fluid (various derivatives which reacted chemically with the low volatility organic liquid, and were generated).
[0005] Although the method of using the mineral salt of a calcium chloride etc. instead of a low volatility organic liquid is shown in JP,6-277470,A as an approach of drying without using a low volatility organic liquid, there is no change in the need of carrying out washing clearance. Moreover, though it is a minute amount, it is apprehensive about the adverse effect which the mineral salt which remained has on a dialysis patient.
[0006] Moreover, the manufacture approach of the hollow fiber which irradiates microwave is shown in JP,11-332980,A as the membranous desiccation approach, performing moist heat treatment by the steam to a hollow fiber. However, since steam treatment is carried out in order to prevent deformation of the film, though it is desiccation, there is a fault which lengthens the drying time, and further, since it is the desiccation after making low volatility organic liquids, such as a glycerol, adhere, the object of reducing the effluent from the film is not attained.
[0007] The hydrophilization film containing the polyvinyl pyrrolidone which carried out desiccation processing to JP,8-52331,A and JP,8-9668,B, without using a low volatility organic liquid is indicated. Although the engine performance which separates a plasma component from blood is indicated by these, since plasma protein penetrates, it turns out that it is not effective as permeable membrane. Moreover, since the polyvinyl pyrrolidone is dried at the temperature decomposed and denatured, in the object of reducing the effluent from the film, it is the process which is not very desirable.
[0008] Moreover, the hollow fiber to which blood made abundance of the polyvinyl pyrrolidone in the film internal surface which contacts directly about 20 - 50% is indicated by JP,6-

296686,A. This shows the humid film for mainly lessening affixes, such as blood protein and a platelet. Therefore, although it is shown that aging of a filtrate rate cannot happen easily since blood protein cannot adhere easily, there is no publication about dialysis engine performance, like the permeability of albumin is low.

[0009] this invention person proposed and did patent application of the approach of drying the humid film which has the specific engine performance, without sinking in low volatility organic liquids, such as a glycerol, and manufacturing the highly efficient blood purification film (application for patent No. 22246 [2001 to]). However, when it was made the shape of a thread as a result of a subsequent examination and dried, it became clear by the core of a thread, and the film of the periphery section that some engine-performance difference arises.

[0010] Then, this invention person proposed and did patent application of the approach of manufacturing the blood purification film which has improved the engine-performance difference in a thread (an application for patent No. 309673 [2001 to], an application for patent No. 309674 [2001 to], application for patent No. 309675 [2001 to]). However, in order to dry two or more threads simultaneously, when microwave irradiation equipment (irradiation reactor) was scaled up as a result of the further examination of this invention persons' after that, also by these approaches, the local temperature rise of a thread happened and it became clear that some threads become poor [the engine performance].

[0011]

[Problem(s) to be Solved by the Invention] The technical problem of this invention is the dryer of the hollow fiber for drying the humid film ****(ed) in the shape of a thread to two or more coincidence by microwave exposure, and is to offer the dryer aiming at preventing the poor engine performance of some [by the local temperature rise in an irradiation reactor] threads, and drying all threads to homogeneity.

[0012]

[Means for Solving the Problem] There was no desiccation film for blood purification which has the dialysis engine performance dried without using the pit hold-back agent leading to the effluent from a module like the above to this invention person's etc. application invention (application for patent No. 22246 [2001 to]). When the cause was dried without using a pit hold-back agent, the damp or wet condition was becoming the film of completely different low engine performance. Then, this invention person etc. produces beforehand the humid film which has the specific engine performance which is a diameter of an osculum in the amount of high water penetration rather than the target engine performance by application in the first half. There is nothing to the former of manufacturing the film which is made dried and contracting this and has the dialysis engine performance of a target. As a result of advancing research wholeheartedly based on the way of thinking that nobody thought of, there were very few effluents and the approach of obtaining the film which has the dialysis engine performance adhesion of blood protein and a platelet excelled [engine performance] in little permselectivity was offered.

[0013] Then, when research was advanced further, this invention persons discovered that dispersion arose in the amount of water penetration, or penetrable ability by the core of a thread, and the film of the periphery section, when manufacturing the blood purification film by the approach of an application for patent No. 22246 [2001 to], and the humid film was made into the shape of a thread and it dried. Then, in order to abolish dispersion, as a result of inquiring wholeheartedly, with devising a desiccation process, it found out that dispersion was suppressed and it newly carried out patent application (an application for patent No. 309673 [2001 to], an application for patent No. 309674 [2001 to], application for patent No. 309675 [2001 to]).

[0014] However, in order to dry two or more threads simultaneously, as a result of scaling up microwave irradiation equipment as a result of a subsequent examination, the thread which becomes poor [the engine performance] was generated. Although a cause is not clear, when the metal member which constitutes the tray used since a thread is fixed by the scale-up heats and discharges, it is guessed that some threads in an irradiation reactor carry out a temperature rise quickly, and it becomes poor [the engine performance]. It is difficult to produce only with plastics, without using a metal, since a tray is used also for receipts and payments of the thread into an irradiation reactor in order for a mechanical strength to fall. Then, in order to prevent heating and discharge of a metal member, as a result of inquiring wholeheartedly, it results in header this invention that some local temperature rises of a thread can be suppressed by passing the fluid (liquid) from which microwave [surplus / except being used for the oscillation (heating of a water molecule) of the water molecule in a thread] is removed efficiently in an irradiation reactor especially on the outskirts of a metal member or the outskirts of it.
[0015] This invention is equipment for drying the humid film ****(ed) in the shape of (1) thread. In a container Namely, a microwave exposure means, The dryer of the hollow fiber characterized by having a means to fix, and to carry in and take out the humid film ****(ed) in the shape of a thread, and a means to pass in a container the liquid whose dielectric loss multipliers are 1-50, (2) Equipment of the above-mentioned (1) publication characterized by having piping for passing the liquid whose dielectric loss multipliers are 1-50 around the metal part in a container, or a metal part, (3) The above (1) characterized by two or more means to irradiate microwave existing, or a manufacturing installation given in (2), (4) The means used in order to fix and take the manufacturing installation given in either of - (3) and (1) (5) thread which are characterized by having a means to ventilate to a thread in and out is fixed. A manufacturing installation given in either of (1) - (4) characterized by having the means furthermore rotated, (6) A manufacturing installation given in either of (1) - (5) characterized by having the function in which a container intercepts microwave, (7) A manufacturing installation given in either of (1) - (6) characterized by having the function which a container keeps the temperature of the gas in a container constant, (8) A manufacturing installation given in either of (1) - (7) characterized by having the function in which a container circulates through the gas in a container, (9) It is related with equipment a manufacturing installation given in either of - (8), and given in either of above-mentioned (1) - (9) whose (1) (10) hollow fiber to which a container is characterized by having the function to replace the gas in a container with an external gas is hollow filament-like blood purification film.
[0016]
[Embodiment of the Invention] Although this invention is not necessarily restricted to the dryer of the hollow filament-like blood purification film, below, it explains the dryer of the hollow filament-like blood purification film (only henceforth the "film" or the "hollow filament-like film") of this invention. Although it is desirable that a pit hold-back agent is not included as for the hollow filament-like blood purification film manufactured using the dryer of this invention, it is not necessarily restricted to it.
[0017] Below, the manufacture approach of the hollow filament-like blood purification film dried using the dryer of this invention is explained first. The manufacture approach of the hollow filament-like blood purification film of this invention manufactures the humid film of a big aperture beforehand in the amount of high water penetration, and has the description to make it dry without carrying out impregnation of the pit hold-back agent after desolventization.
[0018] Usually, it is classified into the inorganic substance with which the pit hold-back agent

used in case the hollow filament-like blood purification film is manufactured is anxious about the toxicity to the organic substance and the body which have viscosity. Since the pit hold-back agent which consists of the organic substance which has viscosity has high viscosity and it is difficult to carry out washing clearance thoroughly, it can change with the cause which remains in the film, is made to increase the elution volume from the film, reacts chemically with the pit hold-back agent which remained further, and produces deleterious material. On the other hand, since it remains in a minute amount also in the pit hold-back agent which consists of an inorganic substance, it is apprehensive about the adverse effect which it has on a dialysis patient.
[0019] The pit hold-back agent as used in the field of this invention is matter put in the hole part in the film in the manufacture process before drying in order to prevent the degradation at the time of desiccation. It is possible by immersing the humid film in the solution containing a pit hold-back agent to put this hold-back agent in the hole part in the film. If even washing and clearance carry out a pit hold-back agent also even for after desiccation, it is possible to hold engine performance, such as the amount of water penetration equivalent to the humid film and rejection, according to the effectiveness of a pit hold-back agent.
[0020] As a pit hold-back agent, the mineral salt of organic compounds, such as ethylene glycol, propylene glycol, a trimethylene glycol, 1, 2-butylene glycol, 1, 3-butylene glycol, and a sucrose fatty acid ester, and a calcium chloride, a sodium carbonate, sodium acetate, magnesium sulfate, a sodium sulfate, a zinc chloride, etc. can be mentioned.
[0021] Moreover, in this invention, the amounts of water penetration are 100mL(s) / (m2 and hr-mmHg) above in the amount of high water penetration, and the humid film of a big aperture means the humid film which the transmission of the polyvinyl pyrrolidone of weight average molecular weight 40,000 exceeds 75%, and has the engine performance whose transmission of the albumin in a cow plasma system is 0.3% or more.
[0022] The permeability of cow plasma albumin can be measured by the following approaches. First, 100 hollow filament-like film with a die length of 20cm is bundled, and a small module is produced. The heparinize cow plasma (heparin 5000 IU/I, protein concentration 6.0 g/dL (deciliter)) warmed to this module at 37 degrees C is passed with the linear velocity of 1.0cm/second to a film internal-surface side, a module enters, and an ultrafiltration is performed for 30 minutes in mean-pressure 50mmHg of ** and ****. It computes permeability by measuring measurement of the concentration of the obtained filtrate and former liquid on the wavelength of 280nm with an ultraviolet spectroscopy photometer, and substituting it for the following formula (1).
Permeability (%) =(absorbance of filtrate) x100/(absorbance of former liquid) (1)
[0023] The transmission of a polyvinyl pyrrolidone is called for by performing the same actuation as measurement of the transmission of cow plasma albumin except having used the water solution to filter as the phosphoric-acid buffer (0.15-mol [// l.], pH7.4) water solution of 3% of the weight of a polyvinyl pyrrolidone (BASF A.G. make K30, weight average molecular weight 40,000), and the module having entered and having set the mean pressure of ** and **** to 200mmHg(s).
[0024] After the humid film of a big aperture making a polysulfone system polymer (only henceforth a "polymer"), a polyvinyl pyrrolidone, and the film production undiluted solution that consists of a solvent breathe out from a double annular nozzle with internal liquid in the amount of high water penetration and passing an air gap, in the manufacture approach made to solidify by the coagulation bath, it can manufacture by using the water solution of the solvent of a polymer for internal liquid.

[0025] Although internal liquid makes a membranous centrum and a membranous internal surface form, it turns out that the aperture of an internal surface becomes large in proportion to the solvent concentration in internal liquid. In this invention, since the permeable membrane of the engine performance of a target is obtained by carrying out drying shrinkage of the humid film, compared with the time of manufacturing the humid film which has the target solvent concentration in internal liquid dialysis-engine performance, it is necessary to make it high concentration.

[0026] What has the repeat unit shown by the following formula (2) or the formula (3) as a polysulfone system polymer used by this invention is mentioned. In addition, Ar in a formula shows the phenyl group of two permutations in the para position, and limits neither about polymerization degree nor especially molecular weight.

-O-Ar-C(CH3)2-Ar-O-Ar-SO2-Ar- (2)

-O-Ar-SO2-Ar- (3)

[0027] Since the hydrophilization effectiveness to the film is as high as the thing of the amount of macromolecules and little and as sufficient effectiveness as the thing of the amount of macromolecules can demonstrate a polyvinyl pyrrolidone, in this invention, a with a weight average molecular weight of 900,000 or more polyvinyl pyrrolidone is used. Although it is necessary to make the polyvinyl pyrrolidone of a large quantity remain in the film in order to give the hydrophilization effectiveness to the film using the polyvinyl pyrrolidone which has weight average molecular weight smaller than 900,000 for this reason, the effluent from the film will increase. Moreover, in order to lower an effluent to reverse, when ullage in the inside of the film of the polyvinyl pyrrolidone of weight average molecular weight smaller than 900,000 was lessened, the hydrophilization effectiveness becomes imperfection and hemodialysis is performed as a result, lowering of filtration velocity with time is caused and sufficient effectiveness cannot be demonstrated.

[0028] Moreover, both the solvents used for the dissolution of a polysulfone system polymer and a polyvinyl pyrrolidone dissolve both these, and are a N-methyl-2-pyrrolidone, N.N-dimethylformamide, N,N-dimethylacetamide, etc.

[0029] Especially if the polymer concentration in a film production undiluted solution is the range of concentration where the film which could produce the film and was obtained has the engine performance as film, it will not be restricted, but it is 10 - 30 % of the weight preferably five to 35% of the weight. In order to attain permeable high ability, the lower one of polymer concentration is good, and its 10 - 25 % of the weight is desirable.

[0030] A still more important thing is the addition of a polyvinyl pyrrolidone, and the mixing ratio of the polyvinyl pyrrolidone to a polymer is 20 - 27 % of the weight still more preferably ten to 27% of the weight preferably 27 or less % of the weight. It is difficult to be in the inclination whose elution volume increases, when the mixing ratio of the polyvinyl pyrrolidone to a polymer exceeds 27 % of the weight, and to obtain the film of sponge structure, since the viscosity of a film production undiluted solution is low at less than 10 % of the weight. Moreover, what is necessary is it to be also possible for to add the 4th component, such as water and a poor solvent, in order to control undiluted solution viscosity and a dissolution condition, and for combination just to perform the class and an addition at any time.

[0031] Water is desirable although the liquid which does not dissolve polymers, such as aliphatic hydrocarbon, such as alcohols; ether;n-hexanes, such as a water; methanol and ethanol, and n-heptane, for example is used as a coagulation bath. Moreover, it is also possible to control a coagulation rate by adding a little the solvent which dissolves a polymer in a coagulation bath. -

30-90 degrees C of 0-90 degrees C of temperature of a coagulation bath are 0-80 degrees C still more preferably preferably. The temperature of a coagulation bath exceeds 90 degrees C, or the surface state of the hollow filament-like film in a coagulation bath cannot be easily stabilized as it is less than -30 degrees C.

[0032] Desiccation after desolventization washing is performed to the thread which is fully carrying out humidity with the gestalt (it is only henceforth called a "thread") of the thread which bundled several hollow filament-like many film by carrying out a microwave exposure. However, since it is suitable for drying the thread of low water content to homogeneity more, in order to prevent deformation and melting of the film by fault heating, when the average water content of a thread becomes 50 - 70% more preferably 20 to 70%, it is desirable [a microwave exposure] to reduce the output of a microwave exposure.

[0033] Furthermore, it is desirable that the difference of the water content of the film in the core and the periphery section of this thread in the event of the average water content of a thread becoming 50 - 70% preferably 20 to 70% is less than 5% in order to suppress dispersion in the engine performance. It is possible at the time of desiccation to make the difference of the water content of the film in the core and the periphery section of a thread less than 5% by ventilating in a thread. Here, the core of a thread means one sixth of the range of a diameter from the central point in the circle configuration cross section of a thread. Moreover, the periphery section of a thread means one sixth of the range of a diameter from a periphery in the circle configuration cross section of a thread.

[0034] Moreover, since it is the same, it is desirable also about the thread at the time of desiccation initiation that the difference of the water content of the film in the core and the periphery section of a thread is less than 10%. If the thread after desolventization is left, since a difference will arise in the water content of the core of a thread, and the periphery section, it is possible by immersing a thread underwater again, just before going into a desiccation process to make the difference of the water content of a thread core and the periphery section less than 10%.

[0035] Here, water content means what is calculated by count by (4) types from the weight (A (g)) of the thread before desiccation (or film), and the weight (B (g)) of a desiccation thread (or film).

Water content (%) =(A-B)x100/B (4)

Furthermore, in order to abolish the difference of the rate of drying of the core of a thread, and the periphery section, it is desirable to ventilate in a thread the dehumidification gas of the temperature which does not exceed 40 degrees C. It means passing a wind between hollow filament-like film as ventilating in a thread. In this invention, ventilating a with a 40-degree-C or more temperature [temperature 120 degrees C or less] dehumidification gas in a thread means performing stoving to a thread at the same time it ventilates in a thread.

[0036] In this invention, the microwave exposure to a thread is performed to two or more bundle coincidence in the sealed irradiation reactor (inside of a container). A thread is made to fix on the tray which consists of a metal member and a nonmetal (for example, plastics). Although the oscillation (heating of a water molecule) of the water molecule in a thread is made to consume microwave, excessive microwave causes heating and discharge of a metal member by one side. This heating and discharge cause the local temperature rise of a thread, and causes some poor engine performance of a thread. In order to lose the poor engine performance, in this invention, it made it possible to remove excessive microwave by passing in piping which installed the liquid with the high absorptive power of microwave in the irradiation reactor.

[0037] As for the absorptive power of microwave, it is desirable to pour a liquid with a big dielectric loss multiplier, since it is proportional to the magnitude of a dielectric loss multiplier, and it is desirable that it is the liquid whose values of a dielectric loss multiplier are 1-50. The liquid with which a dielectric loss multiplier exceeds 50 preferably [since the absorptive power of microwave is low at less than one] is water of a supercooling condition etc., and is not practical.

[0038] The dielectric loss multiplier in this invention means the product of the specific inductive capacity of the matter, and the value of a dielectric dissipation factor measured on the frequency of 2,450MHz (mega hertz). A dielectric loss multiplier as a liquid of 1-50 Alcohols; ethylene glycol, such as water; methyl alcohol and ethyl alcohol, Propylene glycol, a trimethylene glycol, 1, 2-butylene glycol, 1, 3-butylene glycol, 2-butine -1, 4-diol, the 2-methyl -2, 4-PENTA diol, 2-ethyl -1, 3-hexandiol, a glycerol, tetraethylene glycol, Water is the most desirable although the glycol system or glycerol system compound of a polyethylene glycol 200, a polyethylene glycol 300, and polyethylene-glycol 400 grade can be mentioned.

[0039] In this invention, a waveguide means the source of an exposure of microwave. As for a waveguide, it is desirable to use more than one in proportion to the number of threads. Moreover, although the high thing of the output of microwave is desirable, an optimum value changes with the amounts and water content of the film to dry.

[0040] Since a part of PVP in the film can be insolubilized in water by irradiating radiations, such as an electron ray and a gamma ray, at the film after desiccation, it is possible to reduce the elution volume from the film more. Whichever after a modularization of the exposure of a radiation is sufficient as a modularization front stirrup. Moreover, if all PVP in the film is insolubilized, while an elution volume can be reduced, it is not desirable from a leuco PENIA symptom being observed at the time of dialysis.

[0041] With PVP unnecessary in the water as used in the field of this invention, the meltable amount of PVP is deducted from the total amount of PVP in the film in water. The total amount of PVP in the film is easily computable with the elemental analysis of nitrogen and sulfur. Moreover, the amount of PVP meltable in water can be calculated by the following approaches. After dissolving the film thoroughly by the N-methyl-2-pyrrolidone, water is added in the obtained polymer solution and a polysulfone system polymer is settled thoroughly. After putting this polymer solution furthermore, the quantum of meltable PVP can be carried out to water by carrying out the quantum of the amount of PVP in a supernatant with liquid chromatography.

[0042] Especially the dryer of this invention is equipment suitable for drying the humid film which does not contain the pit hold-back agent ****(ed) in the shape of a thread to two or more coincidence, and the film obtained using this equipment It is the desiccation film which does not contain a pit hold-back agent. The permeability of the polyvinyl pyrrolidone of 10-1,000mL/(m2 and hr-mmHg) and weight average molecular weight 40,000 at 75% or less [the amount of water penetration of pure water] And the transmission of the albumin in a cow plasma system is less than 0.3%, and it is the hollow filament-like blood purification film characterized by the variation in each engine performance being still smaller.

[0043] Although the beta 2-microglobulin (molecular weight: 11,800) made into the causative agent for the improvement of dialysis amyloid condition of disease is made to fully penetrate in the latest hemodialysis therapy, the film which has the fractionation nature which does not make most albumin (molecular weight: 67,000) penetrate is called for, and the permeability of albumin [in / in the film of this invention / a cow plasma system] is 0.3% or less. Since it means losing greatly albumin effective in the inside of the body, it is not desirable as hemodialysis film that

the transmission of albumin exceeds 0.3%.
[0044] Moreover, the linear correlation which the amount of water penetration of pure water shows in the following formula (5) at the transmission (A (%)) of a polyvinyl pyrrolidone and the path clearance (B (a part for mL/)) of beta 2-microglobulin in the film of 10mL(s) / (m2 and hr-mmHg) more than exists. Although it is required for path clearance assessment to fabricate and process the module of the dialysis specification which has the effective film surface product of 2 1.5m, with this assessment approach, it is measurable in simple, and it is possible to guess path clearance easily.
B(part for mL/) =0.636A+29.99 (5)
Here, in accordance with the performance-evaluation criteria of Japanese Society for Artificial Organs, dialysis measurement of the path clearance of beta 2-microglobulin is carried out at the module of the effective film surface product of 2 under a part (film internal-surface side) for blood flow rate 200mL/, and the conditions for dialysing fluid flow rate 500mL/(film outside-surface side) 1.5m. Although, as for the path clearance of beta 2-microglobulin, various things are demanded according to a dialysis patient's physical strength, or the percentage of completion of condition of disease and condition of disease, if the transmission of a polyvinyl pyrrolidone exceeds 75%, since the transmission of albumin will exceed 0.3%, the transmission of a polyvinyl pyrrolidone needs to be 75% or less.
[0045] Moreover, since the pit hold-back agent is not being used for the film made by this invention by the production process, the effluent of the pit hold-back agent origin does not exist. Therefore, the absorbance of the effluent test fluid of the film of this invention is less than 0.04, and does not contain a pit hold-back agent in this test fluid. With effluent test fluid, it adjusts here based on hemodialysis apparatus acknowledgement criteria, and after putting 1.5g of desiccation hollow filament-like film cut to 2cm, and distilled-water-for-injection 150mL into the glassware which suits the alkali dissolution test of the glassware trial for injection of a Japanese pharmacopoeia, warming at 70**5 degrees C for 1 hour and removing the film after cooling, what added distilled water and was set to 150mL(s) is meant. An absorbance is measured with an ultraviolet absorption spectrum on the wavelength which shows the maximum absorption wavelength in 220-350nm. Although making an absorbance or less into 0.1 is defined on hemodialysis apparatus acknowledgement criteria, since the film of this invention does not hold a pit hold-back agent, it can attain less than 0.04. Moreover, about the existence of a pit hold-back agent, it is detectable by measuring the thing which condensed or removed [moisture] this test fluid by well-known approaches, such as a gas chromatography, liquid chromatography, differential refractive media, an ultraviolet spectroscopy photometer, an infrared absorptiometry, nuclear-magnetic-resonance spectroscopy, and elemental analysis. Moreover, it is detectable also about whether a pit hold-back agent is included in the film with these measuring methods.
[0046] The film made by this invention consists of a polysulfone system polymer and a polyvinyl pyrrolidone, and the concentration of the polyvinyl pyrrolidone in a film internal surface is 30 - 45 % of the weight. By the polysulfone system film which is the hydrophilic property of the film internal surface which blood touches, and contains a polyvinyl pyrrolidone (only henceforth "PVP"), the PVP concentration of a film internal surface is important for a factor important for membranous haemocompatibility. When the PVP concentration of a film internal surface is too low, a film internal surface shows hydrophobicity, plasma protein tends to adsorb, and the coagulation of blood also tends to take place. That is, it becomes membranous poor haemocompatibility. Conversely, if the PVP concentration of a film internal surface is too

high, the elution volume to the blood system of PVP will increase, and the result which is not desirable will be given for the object and application of this invention. Therefore, the concentration of PVP of the film internal surface in this invention is 30 - 40% of range, and is 33 - 40% preferably.

[0047] The PVP concentration of a film internal surface is determined by the X ray photon spectrum (X-ray Photoelectron spectroscopy, henceforth, XPS). That is, after measurement of XPS of a film internal surface arranges a sample in on a double-sided tape, a cutter cuts it open to fiber shaft orientations, and after extending so that the membranous inside may become a table, it is measured by the usual approach. That is, C1s and O1s, the concentration for which it asked using the relative sensitivity coefficient of equipment attachment from the surface concentration (nitrogen atom concentration) of nitrogen and sulphuric surface concentration (sulfur atom concentration) is said from the integrated intensity of N1s and an S2p spectrum, and when a polysulfone system polymer is the structure of (2) types, it can ask by count by (6) types.

PVP concentration (% of the weight) =C1M1x100/(C1M1+C2M2) (6)

It is here and is C1:nitrogen atom concentration (%).

C2: Sulfur atom concentration (%)

M1 :P Molecular weight of the repeat unit of VP (111)

M2: Molecular weight of the repeat unit of a polysulfone system polymer (442)

[0048] Next, an example of the dryer of this invention is explained with reference to a drawing. The dryer shown in drawing 1 consists of a revolution means (6) which fixes a container (1), a microwave exposure means (2), a means (3) to fix, and to carry in and take out a thread, a thread ventilation means (4), a means (5) to pass the liquid whose dielectric loss multipliers are 1-50, and a means (3) to fix, and to carry in and take out a thread, and is rotated.

[0049] The thread (7) fixed to the means (3) used in order to fix and to carry in and take out a thread is dried by the microwave irradiated from the microwave exposure means (2) within the container (1). A dehumidification gas is passed by the thread with a ventilation means (4) during a microwave exposure. Since a means (5) to pass the liquid whose dielectric loss multipliers are 1-50 is furthermore established in the container, as a result of absorbing surplus microwave and preventing a local temperature rise, all threads can be dried to homogeneity.

[0050] A container (1) has further the function which intercepts (a) microwave, the temperature control means which keeps the temperature in the (b) container constant, a means to circulate through the gas in the (c) container, and a means to permute the gas in the (d) container by the external gas. The function which intercepts microwave not only uses microwave for desiccation of a thread effectively, but is the insurance top need for an operator. Moreover, in order to abolish the engine-performance difference between desiccation batches, it is required to keep the temperature in a container constant. Furthermore, it is possible by replacing the gas in a container with circulation and the exterior to improve drying efficiency.

[0051] Although it is not used since microwave is irradiated at a thread (7), and a configuration and especially magnitude are not limited, in order to dry two or more threads uniformly, as for a microwave exposure means (2), it is desirable to install more than one in a container. The means (3) used in order to fix and to carry in and take out a thread is used in order to fix the location of the thread within a container and to dry efficiently. Furthermore, immobilization and carrying-in / taking-out means (3) can be removed from a dryer, in order to make immobilization and ejection of a thread easy. A thread ventilation means (4) is used in order to ventilate a gas in a thread.

[0052] Although what kind of thing is sufficient as it as long as a means (5) to pass the liquid

whose dielectric loss multipliers are 1-50 is a means by which a liquid can be poured, it is desirable that it is piping made from a nonmetal which makes the interior pass the liquid whose dielectric loss multipliers are 1-50. As for piping for liquid passage, it is desirable that it prepares metal members, such as a metal fixture, on the metal member in an irradiation reactor or the outskirts of it since excessive microwave tends to heat and discharge. The means (6) which fixes a means (3) to fix, and to carry in and take out a thread, and is rotated further is used in order to make the microwave exposure to a thread more equal. The revolution is horizontal.

[0053]

[Example] Although the example of this invention is shown below, this invention is not limited to this.

(Measurement of the amount of platelet adhesion) The following operating procedure performed measurement of the amount of platelet adhesion to the film. Bundle ten hollow filament-like film with a die length of 15cm, produce a small module, and this module is made to pass heparinize Homo sapiens fresh blood for 15 minutes with the linear velocity of 1.0cm/second, and the physiological saline was continuously passed for 1 minute. Next, it computed as LDH activity of per a film surface product (internal-surface conversion) by carrying out the quantum of the lactate dehydrogenase (henceforth "LDH") emitted from the platelet which carried out beating of the hollow filament-like film to 5mm spacing extent, carried out ultrasonic irradiation in the physiological saline which contains the polyethylene-glycol alkylphenyl ether (Wako Pure Chem trade name triton X-100) 0.5%, and adhered to the film front face. Measurement of enzyme activity used the LDH mono-test kit (Boehringer Mannheim and made in Yamanouchi). In addition, it compared with a specimen and coincidence using the film (what was obtained by being immersed in ethanol for one day after the film of the example 1 in front of gamma irradiation was immersed in the sodium hypochlorite with an available chlorine concentration of 1,500 ppm for two days) which does not contain PVP as positive control.

[0054] (Plasma protein amount of adsorption) Except having carried out ultrafiltration time amount in 240 minutes, after the plasma protein amount of adsorption to the film performed the same actuation as the transmissometry of albumin, the physiological saline washed it for 1 minute. Next, it computed as the protein amount of adsorption per film weight by carrying out beating of the hollow filament-like film to 5mm spacing extent, and carrying out the quantum of the plasma protein stirred and extracted in the physiological saline which contains lauryl acid sodium 1.0%. Protein concentration used BCA protein assay (made in Pierce). In addition, it compared with a specimen and coincidence using the film (what was obtained by being immersed in ethanol for one day after the film of the example 1 in front of gamma irradiation was immersed in the sodium hypochlorite with an available chlorine concentration of 1,500 ppm for two days) which does not contain PVP as positive control.

[0055]

[Example 1] (Film production and clearance of a residual solvent) It dissolved in 77.7 % of the weight of N,N-dimethylacetamide, and 18.0 % of the weight (product P-1700 made from Amoco Engineering Polymers) of polysulfones and 4.3 % of the weight (BASF A.G. make K90, weight average molecular weight 1,200,000) of polyvinyl pyrrolidones were used as the uniform solution. Here, the mixing ratio of the polyvinyl pyrrolidone to the polysulfone in a film production undiluted solution was 23.9 % of the weight. This film production undiluted solution was kept at 60 degrees C, and it was immersed to the coagulation bath which is made to breathe out from a spinning port (double annular nozzle 0.1mm - 0.2 mm to 0.3 mm), is made to pass a 0.96m air gap, and consists of 75-degree C water with the internal liquid which consists of a

mixed solution of 30 % of the weight of N,N-dimethylacetamide, and 70 % of the weight of water. At this time, from a spinning port to the coagulation bath was surrounded by the cylinder-like cylinder, the humidity in a cylinder was controlled and temperature was controlled for the nitrogen gas which contained the steam in the cylinder at 51 degrees C 54.5% with the sink. Spinning speed was fixed to a part for 80m/. Here, the ratio of the air gap to spinning speed was 0.012m/(a part for m/). The residual solvent in the film was removed after cutting the rolled-round thread by washing a 80-degree C hot water shower over 2 hours from the cutting plane upper part of a thread (die length of 30cm, 9400 film numbers).

[0056] The equipment shown in drawing 1 is used. (Desiccation of the humid film and insolubilization processing of PVP) The thread after the above-mentioned residual solvent clearance (the water content of the film of a thread core 300% 300%) [water content] The difference of the water content of the film [in / in the water content of the film of the thread periphery section / the core and the periphery section of a thread] has arranged each uniformly by regular intervals 300% by setting a thread to a tray for 90 bundles 0% in a microwave irradiation reactor (3m [/second] wind speed in an irradiation reactor). It fixed with the fixture so that the cutting plane of a thread might surely become a top or the bottom at this time. Furthermore, six waveguides were uniformly fixed by regular intervals, respectively so that microwave might be irradiated by each thread in an irradiation reactor at homogeneity.

[0057] The microwave exposure was carried out for 18 minutes with the microwave output of 30kW (kilowatt) to this thread. The water content of the thread located in the core in an irradiation reactor at this event was 42% (for the water content of the film of a thread core, the water content of the film of 44% and the thread periphery section is 40%). Water content obtained less than 1% of desiccation film (thread) by reducing only the output of microwave to 21kW succeedingly, and carrying out a microwave exposure for 8 more minutes.

[0058] Moreover, the following actuation was performed between the time of desiccation initiation, and the time of desiccation termination.

(1) Water was poured in piping made from a nonmetal installed in the surroundings of the tray in an irradiation reactor.

(2) It was made to rotate at the rate of 4 revolutions of a tray in 1 minute.

(3) The temperature in an irradiation reactor was held at 70**2 degrees C.

(4) Dehumidification air (10% or less of humidity) was ventilated from the lower part of each thread from the lower part of a thread to the upper part at the 4m [/second] wind speed. At this time, the 0.4m [/second] wind speed was measured by the thread average from the upper part of a thread at the time of desiccation initiation. Furthermore, a part of PVP in the film was insolubilized by irradiating the gamma ray of 2.5Mrad(s) at the obtained desiccation film (thread).

[0059] (Performance-evaluation result) Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all threads are shown in a table 1. When the thread (film) equivalent to an average value was used as the module of 2 the effective filtration area of 1.5m and path clearance of beta 2-microglobulin was surveyed, it turned out that it is by part for 32mL/, and it became clear that it is equivalent to a part for path clearance 32.5mL/computed by having substituted it for the formula (5). Furthermore, when this module performed transit measurement of a urea and vitamin B12, the path clearance and the permeability of a urea were part 83% for 185mL(s)/, respectively. Moreover, about vitamin B12, it was part 48% for 95mL(s)/similarly. Measurement is [0044]. It carried out by the same

approach. Moreover, 62% of the total amount of PVP in the film was insoluble in water. As a result of carrying out a membranous eluting material test, the absorbance of effluent test fluid was 0.04 or less. Moreover, since the pit hold-back agent was not used, in effluent test fluid, the pit hold-back agent was contained and was not. Furthermore, as for this film, compared with the positive control film, the amount of platelet adhesion became low (positive control film 43 Unit/m2) clear [that the amount of adhesion of plasma protein is also low] (positive control film 63 mg/g). It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet from the engine performance mentioned above. Moreover, since the transmission of albumin was excellent also in the path clearance of beta 2-microglobulin few, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0060]

[Example 2] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 78 % of the weight 4% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 22.2 % of the weight. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 1. It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet. Moreover, there was little transmission of albumin, and since excelling also in the path clearance of beta 2-microglobulin was suggested, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0061]

[Example 3] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 77.2 % of the weight 4.8% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 26.7 % of the weight. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 1. It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet. Moreover, there was little transmission of albumin, and since excelling also in the path clearance of beta 2-microglobulin was suggested, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0062]

[Example 4] The same actuation as an example 3 was performed except having used the mixing

solution which turns into internal liquid from 52 % of the weight of N,N-dimethylacetamide, and 48 % of the weight of water. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 1. It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet. Moreover, there was little transmission of albumin, and since excelling also in the path clearance of beta 2-microglobulin was suggested, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0063]

[The example 1 of a comparison] The same actuation as an example 1 was performed except there being nothing gamma ray Teru putting. This result is shown in a table 2. It became clear that the absorbance of elution test liquid exceeds 0.04 for elution of PVP. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0064]

[The example 2 of a comparison] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 77.0 % of the weight 5.0% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 27.8 % of the weight. The engine performance of this thread is shown in a table 2. Since the mixing ratio of the polyvinyl pyrrolidone to the polysulfone in a film production undiluted solution is over 27 % of the weight, an elution volume and film internal-surface PVP concentration are increasing. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0065]

[The example 3 of a comparison] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 78.4 % of the weight 3.6% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 20.0 % of the weight. The engine performance of this thread is shown in a table 2. It became clear that the amount of PVP of a film internal surface is less than 30%. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0066]

[The example 4 of a comparison] The same actuation as an example 3 was performed except having used the mixing solution which turns into internal liquid from 60 % of the weight of N,N-dimethylacetamide, and 40 % of the weight of water. The engine performance of this thread is shown in a table 2. This film was engine performance for which the permeability of albumin is over 0.3%, and the permeability of PVP also exceeds 75%. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0067]

[The example 5 of a comparison] The same actuation as an example 1 was performed except having used the mixing solution which turns into internal liquid from 10 % of the weight of N,N-dimethylacetamide, and 90 % of the weight of water. The engine performance of this thread is shown in a table 2. The amount of water penetration of pure water was the engine performance

which is less than 10mL(s)/(m2 and hr-mmHg). The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0068]

[The example 6 of a comparison] The same actuation as an example 1 was performed except having made drying temperature into 170 degrees C. The engine performance of this thread is shown in a table 2. All PVP in the film of this film was insoluble in water. This film is used as the module of 2 the effective filtration area of 1.5m, and it is [0044]. When it was alike and clinical blood assessment was carried out by the shown approach, the leuco PENIA symptom that a dialysis patient's white blood cell count fell temporarily was observed. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0069]

[The example 7 of a comparison] The same actuation as an example 1 was performed except not pouring water in piping made from the nonmetal installed in the surroundings of the tray in an irradiation reactor, and the tray lower part. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 3. Discharge was observed from the metal member of the tray between microwave exposures. In the thread which exists on the outskirts of a metal fixture of a tray with this discharge and heating, that whose amount of water penetration is 0 (zero) was seen, and it became clear that the thread of the poor engine performance is generated clearly.

[0070]

[A table 1]

	実施例1		実施例2		実施例3		実施例4	
	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能の糸束の値
膜内径(μm)	195	195	200	200	195	195	196	196
膜外径(μm)	285	286	285	290	285	283	285	289
透水量(mL/(m²·hr·mmHg))	22	19	16	15	23	20	420	400
アルブミンの透過率(%)	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下
PVPの透過率(%)	4	4	4	4	5	5	72	72
膜内表面PVP量度(重量%)	35	35	30	30	44	44	36	35
水に不溶であるPVPの有無	有り	有り	有り	有り	有り	有り	有り	有り
溶出物試験液の紫光度	0.022	0.022	0.020	0.020	0.035	0.035	0.022	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し	無し	無し	無し	無し	無し	無し
血小板粘着量(LDH·Unit/m²)	15.6	15.7	17.7	17.5	4.1	4.1	14.0	14.1
血漿タンパク質吸着量(mg/g)	2.2	2.2	5.5	5.6	1.9	1.9	2.0	2.0
乾燥前膜糊膜の透水量(mL/(m²·hr·mmHg))	190	190	170	170	260	260	3100	3100
乾燥前膜糊膜のアルブミンの透過率(%)	0.32	0.32	0.34	0.34	0.35	0.35	0.51	0.51
乾燥前膜糊膜のPVPの透過率(%)	77	77	84	84	84	84	99	99

[0071]
[A table 2]

[0072]
[A table 3]

[0073]
[Effect of the Invention] According to the dryer of this invention, a hollow fiber can be dried, without producing the poor engine performance in some threads, when drying the humid film ****(ed) in the shape of a thread to two or more bundle coincidence by microwave exposure. The manufactured hollow fiber has very few elution volumes from the film, and since it has the outstanding dialysis engine performance with little adhesion of blood protein and a platelet, it can be used for a remedy application, a medical-application way, and a general industrial application.

TECHNICAL FIELD

[Field of the Invention] This invention relates to the dryer of a hollow fiber. More, this invention is equipment for drying the humid film ****(ed) in the shape of a thread by microwave exposure at two or more bundle coincidence, and relates to the dryer aiming at preventing the poor engine performance of some [by the local temperature rise in an irradiation reactor] threads, and drying all threads to homogeneity at a detail.

PRIOR ART

[Description of the Prior Art] The technique of using the film which has alternative permeability progresses splendidly in recent years, and utilization in extensive fields, such as a separation filter of a gas or a liquid, hemodialyzer in the medical field, a blood filter, and a constituent-of-blood selection separation filter, is progressing until now. As an ingredient of this film, polymers, such as cellulose types (a regenerated-cellulose system, a cellulose acetate system, chemistry denaturation cellulose type, etc.), a polyacrylonitrile system, a polymethylmethacrylate system, a polysulfone system, a polyethylene vinyl alcohol system, and a polyamide system, have been used. Among these, since haemocompatibility of a polysulfone system polymer improves by in addition to the thermal stability, acid-proof, and alkali resistance adding a hydrophilization agent to a film production undiluted solution, and producing a film to it, it was observed as a semipermeable membrane raw material, and research has been advanced.

[0003] On the other hand, in order to paste up the film and to produce a module, it is necessary to dry the film but, and if the porous membrane which consists of an organic macromolecule, the permeable membrane which consists of hydrophobic polymers, such as a polysulfone system, especially, and ultrafiltration membrane are dried after film production, it is known that the amount of water penetration will fall remarkably compared with desiccation before. Therefore, the film always needed to be dealt with in the damp or wet condition and the condition of having made water immersed.

[0004] The approach taken from the former as this cure was putting low volatility organic liquids, such as a glycerol, in the hole part in porous membrane after film production and before desiccation. However, since hyperviscosity [a low volatility organic liquid] generally, although washing clearance took time amount, module molding of the film was carried out and after washing was a minute amount, the problem was to see the effluent of the low volatility organic liquid origin etc. in module mounting fluid (various derivatives which reacted chemically with the low volatility organic liquid, and were generated).

[0005] Although the method of using the mineral salt of a calcium chloride etc. instead of a low volatility organic liquid is shown in JP,6-277470,A as an approach of drying without using a low volatility organic liquid, there is no change in the need of carrying out washing clearance. Moreover, though it is a minute amount, it is apprehensive about the adverse effect which the mineral salt which remained has on a dialysis patient.

[0006] Moreover, the manufacture approach of the hollow fiber which irradiates microwave is shown in JP,11-332980,A as the membranous desiccation approach, performing moist heat treatment by the steam to a hollow fiber. However, since steam treatment is carried out in order to prevent deformation of the film, though it is desiccation, there is a fault which lengthens the drying time, and further, since it is the desiccation after making low volatility organic liquids, such as a glycerol, adhere, the object of reducing the effluent from the film is not attained.

[0007] The hydrophilization film containing the polyvinyl pyrrolidone which carried out desiccation processing to JP,8-52331,A and JP,8-9668,B, without using a low volatility organic liquid is indicated. Although the engine performance which separates a plasma component from blood is indicated by these, since plasma protein penetrates, it turns out that it is not effective as permeable membrane. Moreover, since the polyvinyl pyrrolidone is dried at the temperature decomposed and denatured, in the object of reducing the effluent from the film, it is the process

which is not very desirable.
[0008] Moreover, the hollow fiber to which blood made abundance of the polyvinyl pyrrolidone in the film internal surface which contacts directly about 20 - 50% is indicated by JP,6-296686,A. This shows the humid film for mainly lessening affixes, such as blood protein and a platelet. Therefore, although it is shown that aging of a filtrate rate cannot happen easily since blood protein cannot adhere easily, there is no publication about dialysis engine performance, like the permeability of albumin is low.
[0009] this invention person proposed and did patent application of the approach of drying the humid film which has the specific engine performance, without sinking in low volatility organic liquids, such as a glycerol, and manufacturing the highly efficient blood purification film (application for patent No. 22246 [2001 to]). However, when it was made the shape of a thread as a result of a subsequent examination and dried, it became clear by the core of a thread, and the film of the periphery section that some engine-performance difference arises.
[0010] Then, this invention person proposed and did patent application of the approach of manufacturing the blood purification film which has improved the engine-performance difference in a thread (an application for patent No. 309673 [2001 to], an application for patent No. 309674 [2001 to], application for patent No. 309675 [2001 to]). However, in order to dry two or more threads simultaneously, when microwave irradiation equipment (irradiation reactor) was scaled up as a result of the further examination of this invention persons' after that, also by these approaches, the local temperature rise of a thread happened and it became clear that some threads become poor [the engine performance].

EFFECT OF THE INVENTION

[Effect of the Invention] According to the dryer of this invention, a hollow fiber can be dried, without producing the poor engine performance in some threads, when drying the humid film ****(ed) in the shape of a thread to two or more bundle coincidence by microwave exposure. The manufactured hollow fiber has very few elution volumes from the film, and since it has the outstanding dialysis engine performance with little adhesion of blood protein and a platelet, it can be used for a remedy application, a medical-application way, and a general industrial application.

TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] The technical problem of this invention is the dryer of the hollow fiber for drying the humid film ****(ed) in the shape of a thread to two or more coincidence by microwave exposure, and is to offer the dryer aiming at preventing the poor engine performance of some [by the local temperature rise in an irradiation reactor] threads, and drying all threads to homogeneity.

MEANS

[Means for Solving the Problem] There was no desiccation film for blood purification which has the dialysis engine performance dried without using the pit hold-back agent leading to the effluent from a module like the above to this invention person's etc. application invention (application for patent No. 22246 [2001 to]). When the cause was dried without using a pit hold-back agent, the damp or wet condition was becoming the film of completely different low engine performance. Then, this invention person etc. produces beforehand the humid film which has the specific engine performance which is a diameter of an osculum in the amount of high water penetration rather than the target engine performance by application in the first half. There is nothing to the former of manufacturing the film which is made dried and contracting this and has the dialysis engine performance of a target. As a result of advancing research wholeheartedly based on the way of thinking that nobody thought of, there were very few effluents and the approach of obtaining the film which has the dialysis engine performance adhesion of blood protein and a platelet excelled [engine performance] in little permselectivity was offered.
[0013] Then, when research was advanced further, this invention persons discovered that dispersion arose in the amount of water penetration, or penetrable ability by the core of a thread, and the film of the periphery section, when manufacturing the blood purification film by the approach of an application for patent No. 22246 [2001 to], and the humid film was made into the shape of a thread and it dried. Then, in order to abolish dispersion, as a result of inquiring wholeheartedly, with devising a desiccation process, it found out that dispersion was suppressed and it newly carried out patent application (an application for patent No. 309673 [2001 to], an application for patent No. 309674 [2001 to], application for patent No. 309675 [2001 to]).
[0014] However, in order to dry two or more threads simultaneously, as a result of scaling up microwave irradiation equipment as a result of a subsequent examination, the thread which becomes poor [the engine performance] was generated. Although a cause is not clear, when the metal member which constitutes the tray used since a thread is fixed by the scale-up heats and discharges, it is guessed that some threads in an irradiation reactor carry out a temperature rise quickly, and it becomes poor [the engine performance]. It is difficult to produce only with plastics, without using a metal, since a tray is used also for receipts and payments of the thread into an irradiation reactor in order for a mechanical strength to fall. Then, in order to prevent heating and discharge of a metal member, as a result of inquiring wholeheartedly, it results in header this invention that some local temperature rises of a thread can be suppressed by passing the fluid (liquid) from which microwave [surplus / except being used for the oscillation (heating of a water molecule) of the water molecule in a thread] is removed efficiently in an irradiation reactor especially on the outskirts of a metal member or the outskirts of it.
[0015] This invention is equipment for drying the humid film ****(ed) in the shape of (1) thread. In a container Namely, a microwave exposure means, The dryer of the hollow fiber characterized by having a means to fix, and to carry in and take out the humid film ****(ed) in the shape of a thread, and a means to pass in a container the liquid whose dielectric loss multipliers are 1-50, (2) Equipment of the above-mentioned (1) publication characterized by having piping for passing the liquid whose dielectric loss multipliers are 1-50 around the metal part in a container, or a metal part, (3) The above (1) characterized by two or more means to irradiate microwave existing, or a manufacturing installation given in (2), (4) The means used in order to fix and take the manufacturing installation given in either of - (3) and (1) (5) thread which are characterized

by having a means to ventilate to a thread in and out is fixed. A manufacturing installation given in either of (1) - (4) characterized by having the means furthermore rotated, (6) A manufacturing installation given in either of (1) - (5) characterized by having the function in which a container intercepts microwave, (7) A manufacturing installation given in either of (1) - (6) characterized by having the function which a container keeps the temperature of the gas in a container constant, (8) A manufacturing installation given in either of (1) - (7) characterized by having the function in which a container circulates through the gas in a container, (9) It is related with equipment a manufacturing installation given in either of - (8), and given in either of above-mentioned (1) - (9) whose (1) (10) hollow fiber to which a container is characterized by having the function to replace the gas in a container with an external gas is hollow filament-like blood purification film.

[0016]

[Embodiment of the Invention] Although this invention is not necessarily restricted to the dryer of the hollow filament-like blood purification film, below, it explains the dryer of the hollow filament-like blood purification film (only henceforth the "film" or the "hollow filament-like film") of this invention. Although it is desirable that a pit hold-back agent is not included as for the hollow filament-like blood purification film manufactured using the dryer of this invention, it is not necessarily restricted to it.

[0017] Below, the manufacture approach of the hollow filament-like blood purification film dried using the dryer of this invention is explained first. The manufacture approach of the hollow filament-like blood purification film of this invention manufactures the humid film of a big aperture beforehand in the amount of high water penetration, and has the description to make it dry without carrying out impregnation of the pit hold-back agent after desolventization.

[0018] Usually, it is classified into the inorganic substance with which the pit hold-back agent used in case the hollow filament-like blood purification film is manufactured is anxious about the toxicity to the organic substance and the body which have viscosity. Since the pit hold-back agent which consists of the organic substance which has viscosity has high viscosity and it is difficult to carry out washing clearance thoroughly, it can change with the cause which remains in the film, is made to increase the elution volume from the film, reacts chemically with the pit hold-back agent which remained further, and produces deleterious material. On the other hand, since it remains in a minute amount also in the pit hold-back agent which consists of an inorganic substance, it is apprehensive about the adverse effect which it has on a dialysis patient.

[0019] The pit hold-back agent as used in the field of this invention is matter put in the hole part in the film in the manufacture process before drying in order to prevent the degradation at the time of desiccation. It is possible by immersing the humid film in the solution containing a pit hold-back agent to put this hold-back agent in the hole part in the film. If even washing and clearance carry out a pit hold-back agent also even for after desiccation, it is possible to hold engine performance, such as the amount of water penetration equivalent to the humid film and rejection, according to the effectiveness of a pit hold-back agent.

[0020] As a pit hold-back agent, the mineral salt of organic compounds, such as ethylene glycol, propylene glycol, a trimethylene glycol, 1, 2-butylene glycol, 1, 3-butylene glycol, and a sucrose fatty acid ester, and a calcium chloride, a sodium carbonate, sodium acetate, magnesium sulfate, a sodium sulfate, a zinc chloride, etc. can be mentioned.

[0021] Moreover, in this invention, the amounts of water penetration are 100mL(s) / (m2 and hr-mmHg) above in the amount of high water penetration, and the humid film of a big aperture means the humid film which the transmission of the polyvinyl pyrrolidone of weight average

molecular weight 40,000 exceeds 75%, and has the engine performance whose transmission of the albumin in a cow plasma system is 0.3% or more.
[0022] The permeability of cow plasma albumin can be measured by the following approaches. First, 100 hollow filament-like film with a die length of 20cm is bundled, and a small module is produced. The heparinize cow plasma (heparin 5000 IU/l, protein concentration 6.0 g/dL (deciliter)) warmed to this module at 37 degrees C is passed with the linear velocity of 1.0cm/second to a film internal-surface side, a module enters, and an ultrafiltration is performed for 30 minutes in mean-pressure 50mmHg of ** and ****. It computes permeability by measuring measurement of the concentration of the obtained filtrate and former liquid on the wavelength of 280nm with an ultraviolet spectroscopy photometer, and substituting it for the following formula (1).
Permeability (%) =(absorbance of filtrate) x100/(absorbance of former liquid) (1)
[0023] The transmission of a polyvinyl pyrrolidone is called for by performing the same actuation as measurement of the transmission of cow plasma albumin except having used the water solution to filter as the phosphoric-acid buffer (0.15-mol [// l.], pH7.4) water solution of 3% of the weight of a polyvinyl pyrrolidone (BASF A.G. make K30, weight average molecular weight 40,000), and the module having entered and having set the mean pressure of ** and **** to 200mmHg(s).
[0024] After the humid film of a big aperture making a polysulfone system polymer (only henceforth a "polymer"), a polyvinyl pyrrolidone, and the film production undiluted solution that consists of a solvent breathe out from a double annular nozzle with internal liquid in the amount of high water penetration and passing an air gap, in the manufacture approach made to solidify by the coagulation bath, it can manufacture by using the water solution of the solvent of a polymer for internal liquid.
[0025] Although internal liquid makes a membranous centrum and a membranous internal surface form, it turns out that the aperture of an internal surface becomes large in proportion to the solvent concentration in internal liquid. In this invention, since the permeable membrane of the engine performance of a target is obtained by carrying out drying shrinkage of the humid film, compared with the time of manufacturing the humid film which has the target solvent concentration in internal liquid dialysis-engine performance, it is necessary to make it high concentration.
[0026] What has the repeat unit shown by the following formula (2) or the formula (3) as a polysulfone system polymer used by this invention is mentioned. In addition, Ar in a formula shows the phenyl group of two permutations in the para position, and limits neither about polymerization degree nor especially molecular weight.
-O-Ar-C(CH3)2-Ar-O-Ar-SO2-Ar- (2)
-O-Ar-SO2-Ar- (3)
[0027] Since the hydrophilization effectiveness to the film is as high as the thing of the amount of macromolecules and little and as sufficient effectiveness as the thing of the amount of macromolecules can demonstrate a polyvinyl pyrrolidone, in this invention, a with a weight average molecular weight of 900,000 or more polyvinyl pyrrolidone is used. Although it is necessary to make the polyvinyl pyrrolidone of a large quantity remain in the film in order to give the hydrophilization effectiveness to the film using the polyvinyl pyrrolidone which has weight average molecular weight smaller than 900,000 for this reason, the effluent from the film will increase. Moreover, in order to lower an effluent to reverse, when ullage in the inside of the film of the polyvinyl pyrrolidone of weight average molecular weight smaller than 900,000 was

lessened, the hydrophilization effectiveness becomes imperfection and hemodialysis is performed as a result, lowering of filtration velocity with time is caused and sufficient effectiveness cannot be demonstrated.

[0028] Moreover, both the solvents used for the dissolution of a polysulfone system polymer and a polyvinyl pyrrolidone dissolve both these, and are a N-methyl-2-pyrrolidone, N.N-dimethylformamide, N,N-dimethylacetamide, etc.

[0029] Especially if the polymer concentration in a film production undiluted solution is the range of concentration where the film which could produce the film and was obtained has the engine performance as film, it will not be restricted, but it is 10 - 30 % of the weight preferably five to 35% of the weight. In order to attain permeable high ability, the lower one of polymer concentration is good, and its 10 - 25 % of the weight is desirable.

[0030] A still more important thing is the addition of a polyvinyl pyrrolidone, and the mixing ratio of the polyvinyl pyrrolidone to a polymer is 20 - 27 % of the weight still more preferably ten to 27% of the weight preferably 27 or less % of the weight. It is difficult to be in the inclination whose elution volume increases, when the mixing ratio of the polyvinyl pyrrolidone to a polymer exceeds 27 % of the weight, and to obtain the film of sponge structure, since the viscosity of a film production undiluted solution is low at less than 10 % of the weight. Moreover, what is necessary is it to be also possible for to add the 4th component, such as water and a poor solvent, in order to control undiluted solution viscosity and a dissolution condition, and for combination just to perform the class and an addition at any time.

[0031] Water is desirable although the liquid which does not dissolve polymers, such as aliphatic hydrocarbon, such as alcohols; ether;n-hexanes, such as a water; methanol and ethanol, and n-heptane, for example is used as a coagulation bath. Moreover, it is also possible to control a coagulation rate by adding a little the solvent which dissolves a polymer in a coagulation bath. -30-90 degrees C of 0-90 degrees C of temperature of a coagulation bath are 0-80 degrees C still more preferably preferably. The temperature of a coagulation bath exceeds 90 degrees C, or the surface state of the hollow filament-like film in a coagulation bath cannot be easily stabilized as it is less than -30 degrees C.

[0032] Desiccation after desolventization washing is performed to the thread which is fully carrying out humidity with the gestalt (it is only henceforth called a "thread") of the thread which bundled several hollow filament-like many film by carrying out a microwave exposure. However, since it is suitable for drying the thread of low water content to homogeneity more, in order to prevent deformation and melting of the film by fault heating, when the average water content of a thread becomes 50 - 70% more preferably 20 to 70%, it is desirable [a microwave exposure] to reduce the output of a microwave exposure.

[0033] Furthermore, it is desirable that the difference of the water content of the film in the core and the periphery section of this thread in the event of the average water content of a thread becoming 50 - 70% preferably 20 to 70% is less than 5% in order to suppress dispersion in the engine performance. It is possible at the time of desiccation to make the difference of the water content of the film in the core and the periphery section of a thread less than 5% by ventilating in a thread. Here, the core of a thread means one sixth of the range of a diameter from the central point in the circle configuration cross section of a thread. Moreover, the periphery section of a thread means one sixth of the range of a diameter from a periphery in the circle configuration cross section of a thread.

[0034] Moreover, since it is the same, it is desirable also about the thread at the time of desiccation initiation that the difference of the water content of the film in the core and the

periphery section of a thread is less than 10%. If the thread after desolventization is left, since a difference will arise in the water content of the core of a thread, and the periphery section, it is possible by immersing a thread underwater again, just before going into a desiccation process to make the difference of the water content of a thread core and the periphery section less than 10%.

[0035] Here, water content means what is calculated by count by (4) types from the weight (A (g)) of the thread before desiccation (or film), and the weight (B (g)) of a desiccation thread (or film).

Water content (%) =(A-B)x100/B (4)

Furthermore, in order to abolish the difference of the rate of drying of the core of a thread, and the periphery section, it is desirable to ventilate in a thread the dehumidification gas of the temperature which does not exceed 40 degrees C. It means passing a wind between hollow filament-like film as ventilating in a thread. In this invention, ventilating a with a 40-degree-C or more temperature [temperature 120 degrees C or less] dehumidification gas in a thread means performing stoving to a thread at the same time it ventilates in a thread.

[0036] In this invention, the microwave exposure to a thread is performed to two or more bundle coincidence in the sealed irradiation reactor (inside of a container). A thread is made to fix on the tray which consists of a metal member and a nonmetal (for example, plastics). Although the oscillation (heating of a water molecule) of the water molecule in a thread is made to consume microwave, excessive microwave causes heating and discharge of a metal member by one side. This heating and discharge cause the local temperature rise of a thread, and causes some poor engine performance of a thread. In order to lose the poor engine performance, in this invention, it made it possible to remove excessive microwave by passing in piping which installed the liquid with the high absorptive power of microwave in the irradiation reactor.

[0037] As for the absorptive power of microwave, it is desirable to pour a liquid with a big dielectric loss multiplier, since it is proportional to the magnitude of a dielectric loss multiplier, and it is desirable that it is the liquid whose values of a dielectric loss multiplier are 1-50. The liquid with which a dielectric loss multiplier exceeds 50 preferably [since the absorptive power of microwave is low at less than one] is water of a supercooling condition etc., and is not practical.

[0038] The dielectric loss multiplier in this invention means the product of the specific inductive capacity of the matter, and the value of a dielectric dissipation factor measured on the frequency of 2,450MHz (mega hertz). A dielectric loss multiplier as a liquid of 1-50 Alcohols; ethylene glycol, such as water; methyl alcohol and ethyl alcohol, Propylene glycol, a trimethylene glycol, 1, 2-butylene glycol, 1, 3-butylene glycol, 2-butine -1, 4-diol, the 2-methyl -2, 4-PENTA diol, 2-ethyl -1, 3-hexandiol, a glycerol, tetraethylene glycol, Water is the most desirable although the glycol system or glycerol system compound of a polyethylene glycol 200, a polyethylene glycol 300, and polyethylene-glycol 400 grade can be mentioned.

[0039] In this invention, a waveguide means the source of an exposure of microwave. As for a waveguide, it is desirable to use more than one in proportion to the number of threads. Moreover, although the high thing of the output of microwave is desirable, an optimum value changes with the amounts and water content of the film to dry.

[0040] Since a part of PVP in the film can be insolubilized in water by irradiating radiations, such as an electron ray and a gamma ray, at the film after desiccation, it is possible to reduce the elution volume from the film more. Whichever after a modularization of the exposure of a radiation is sufficient as a modularization front stirrup. Moreover, if all PVP in the film is

insolubilized, while an elution volume can be reduced, it is not desirable from a leuco PENIA symptom being observed at the time of dialysis.
[0041] With PVP unnecessary in the water as used in the field of this invention, the meltable amount of PVP is deducted from the total amount of PVP in the film in water. The total amount of PVP in the film is easily computable with the elemental analysis of nitrogen and sulfur. Moreover, the amount of PVP meltable in water can be calculated by the following approaches. After dissolving the film thoroughly by the N-methyl-2-pyrrolidone, water is added in the obtained polymer solution and a polysulfone system polymer is settled thoroughly. After putting this polymer solution furthermore, the quantum of meltable PVP can be carried out to water by carrying out the quantum of the amount of PVP in a supernatant with liquid chromatography.
[0042] Especially the dryer of this invention is equipment suitable for drying the humid film which does not contain the pit hold-back agent ****(ed) in the shape of a thread to two or more coincidence, and the film obtained using this equipment It is the desiccation film which does not contain a pit hold-back agent. The permeability of the polyvinyl pyrrolidone of 10-1,000mL/(m2 and hr-mmHg) and weight average molecular weight 40,000 at 75% or less [the amount of water penetration of pure water] And the transmission of the albumin in a cow plasma system is less than 0.3%, and it is the hollow filament-like blood purification film characterized by the variation in each engine performance being still smaller.
[0043] Although the beta 2-microglobulin (molecular weight: 11,800) made into the causative agent for the improvement of dialysis amyloid condition of disease is made to fully penetrate in the latest hemodialysis therapy, the film which has the fractionation nature which does not make most albumin (molecular weight: 67,000) penetrate is called for, and the permeability of albumin [in / in the film of this invention / a cow plasma system] is 0.3% or less. Since it means losing greatly albumin effective in the inside of the body, it is not desirable as hemodialysis film that the transmission of albumin exceeds 0.3%.
[0044] Moreover, the linear correlation which the amount of water penetration of pure water shows in the following formula (5) at the transmission (A (%)) of a polyvinyl pyrrolidone and the path clearance (B (a part for mL/)) of beta 2-microglobulin in the film of 10mL(s) / (m2 and hr-mmHg) more than exists. Although it is required for path clearance assessment to fabricate and process the module of the dialysis specification which has the effective film surface product of 2 1.5m, with this assessment approach, it is measurable in simple, and it is possible to guess path clearance easily.
B(part for mL/) =0.636A+29.99 (5)
Here, in accordance with the performance-evaluation criteria of Japanese Society for Artificial Organs, dialysis measurement of the path clearance of beta 2-microglobulin is carried out at the module of the effective film surface product of 2 under a part (film internal-surface side) for blood flow rate 200mL/, and the conditions for dialysing fluid flow rate 500mL/(film outside-surface side) 1.5m. Although, as for the path clearance of beta 2-microglobulin, various things are demanded according to a dialysis patient's physical strength, or the percentage of completion of condition of disease and condition of disease, if the transmission of a polyvinyl pyrrolidone exceeds 75%, since the transmission of albumin will exceed 0.3%, the transmission of a polyvinyl pyrrolidone needs to be 75% or less.
[0045] Moreover, since the pit hold-back agent is not being used for the film made by this invention by the production process, the effluent of the pit hold-back agent origin does not exist. Therefore, the absorbance of the effluent test fluid of the film of this invention is less than 0.04, and does not contain a pit hold-back agent in this test fluid. With effluent test fluid, it adjusts

here based on hemodialysis apparatus acknowledgement criteria, and after putting 1.5g of desiccation hollow filament-like film cut to 2cm, and distilled-water-for-injection 150mL into the glassware which suits the alkali dissolution test of the glassware trial for injection of a Japanese pharmacopoeia, warming at 70**5 degrees C for 1 hour and removing the film after cooling, what added distilled water and was set to 150mL(s) is meant. An absorbance is measured with an ultraviolet absorption spectrum on the wavelength which shows the maximum absorption wavelength in 220-350nm. Although making an absorbance or less into 0.1 is defined on hemodialysis apparatus acknowledgement criteria, since the film of this invention does not hold a pit hold-back agent, it can attain less than 0.04. Moreover, about the existence of a pit hold-back agent, it is detectable by measuring the thing which condensed or removed [moisture] this test fluid by well-known approaches, such as a gas chromatography, liquid chromatography, differential refractive media, an ultraviolet spectroscopy photometer, an infrared absorptiometry, nuclear-magnetic-resonance spectroscopy, and elemental analysis. Moreover, it is detectable also about whether a pit hold-back agent is included in the film with these measuring methods.

[0046] The film made by this invention consists of a polysulfone system polymer and a polyvinyl pyrrolidone, and the concentration of the polyvinyl pyrrolidone in a film internal surface is 30 - 45 % of the weight. By the polysulfone system film which is the hydrophilic property of the film internal surface which blood touches, and contains a polyvinyl pyrrolidone (only henceforth "PVP"), the PVP concentration of a film internal surface is important for a factor important for membranous haemocompatibility. When the PVP concentration of a film internal surface is too low, a film internal surface shows hydrophobicity, plasma protein tends to adsorb, and the coagulation of blood also tends to take place. That is, it becomes membranous poor haemocompatibility. Conversely, if the PVP concentration of a film internal surface is too high, the elution volume to the blood system of PVP will increase, and the result which is not desirable will be given for the object and application of this invention. Therefore, the concentration of PVP of the film internal surface in this invention is 30 - 40% of range, and is 33 - 40% preferably.

[0047] The PVP concentration of a film internal surface is determined by the X ray photon spectrum (X-ray Photoelectron spectroscopy, henceforth, XPS). That is, after measurement of XPS of a film internal surface arranges a sample in on a double-sided tape, a cutter cuts it open to fiber shaft orientations, and after extending so that the membranous inside may become a table, it is measured by the usual approach. That is, C1s and O1s, the concentration for which it asked using the relative sensitivity coefficient of equipment attachment from the surface concentration (nitrogen atom concentration) of nitrogen and sulphuric surface concentration (sulfur atom concentration) is said from the integrated intensity of N1s and an S2p spectrum, and when a polysulfone system polymer is the structure of (2) types, it can ask by count by (6) types.

PVP concentration (% of the weight) =C1M1x100/(C1M1+C2M2) (6)

It is here and is C1:nitrogen atom concentration (%).

C2: Sulfur atom concentration (%)

M1 </SUB> :P Molecular weight of the repeat unit of VP (111)

M2: Molecular weight of the repeat unit of a polysulfone system polymer (442)

[0048] Next, an example of the dryer of this invention is explained with reference to a drawing. The dryer shown in drawing 1 consists of a revolution means (6) which fixes a container (1), a microwave exposure means (2), a means (3) to fix, and to carry in and take out a thread, a thread ventilation means (4), a means (5) to pass the liquid whose dielectric loss multipliers are 1-50,

and a means (3) to fix, and to carry in and take out a thread, and is rotated.
[0049] The thread (7) fixed to the means (3) used in order to fix and to carry in and take out a thread is dried by the microwave irradiated from the microwave exposure means (2) within the container (1). A dehumidification gas is passed by the thread with a ventilation means (4) during a microwave exposure. Since a means (5) to pass the liquid whose dielectric loss multipliers are 1-50 is furthermore established in the container, as a result of absorbing surplus microwave and preventing a local temperature rise, all threads can be dried to homogeneity.
[0050] A container (1) has further the function which intercepts (a) microwave, the temperature control means which keeps the temperature in the (b) container constant, a means to circulate through the gas in the (c) container, and a means to permute the gas in the (d) container by the external gas. The function which intercepts microwave not only uses microwave for desiccation of a thread effectively, but is the insurance top need for an operator. Moreover, in order to abolish the engine-performance difference between desiccation batches, it is required to keep the temperature in a container constant. Furthermore, it is possible by replacing the gas in a container with circulation and the exterior to improve drying efficiency.
[0051] Although it is not used since microwave is irradiated at a thread (7), and a configuration and especially magnitude are not limited, in order to dry two or more threads uniformly, as for a microwave exposure means (2), it is desirable to install more than one in a container. The means (3) used in order to fix and to carry in and take out a thread is used in order to fix the location of the thread within a container and to dry efficiently. Furthermore, immobilization and carrying-in / taking-out means (3) can be removed from a dryer, in order to make immobilization and ejection of a thread easy. A thread ventilation means (4) is used in order to ventilate a gas in a thread.
[0052] Although what kind of thing is sufficient as it as long as a means (5) to pass the liquid whose dielectric loss multipliers are 1-50 is a means by which a liquid can be poured, it is desirable that it is piping made from a nonmetal which makes the interior pass the liquid whose dielectric loss multipliers are 1-50. As for piping for liquid passage, it is desirable that it prepares metal members, such as a metal fixture, on the metal member in an irradiation reactor or the outskirts of it since excessive microwave tends to heat and discharge. The means (6) which fixes a means (3) to fix, and to carry in and take out a thread, and is rotated further is used in order to make the microwave exposure to a thread more equal. The revolution is horizontal.

EXAMPLE

[Example] Although the example of this invention is shown below, this invention is not limited to this.
(Measurement of the amount of platelet adhesion) The following operating procedure performed measurement of the amount of platelet adhesion to the film. Bundle ten hollow filament-like film with a die length of 15cm, produce a small module, and this module is made to pass heparinize Homo sapiens fresh blood for 15 minutes with the linear velocity of 1.0cm/second, and the physiological saline was continuously passed for 1 minute. Next, it computed as LDH activity of per a film surface product (internal-surface conversion) by carrying out the quantum of the lactate dehydrogenase (henceforth "LDH") emitted from the platelet which carried out beating of the hollow filament-like film to 5mm spacing extent, carried out ultrasonic irradiation in the

physiological saline which contains the polyethylene-glycol alkylphenyl ether (Wako Pure Chem trade name triton X-100) 0.5%, and adhered to the film front face. Measurement of enzyme activity used the LDH mono-test kit (Boehringer Mannheim and made in Yamanouchi). In addition, it compared with a specimen and coincidence using the film (what was obtained by being immersed in ethanol for one day after the film of the example 1 in front of gamma irradiation was immersed in the sodium hypochlorite with an available chlorine concentration of 1,500 ppm for two days) which does not contain PVP as positive control.

[0054] (Plasma protein amount of adsorption) Except having carried out ultrafiltration time amount in 240 minutes, after the plasma protein amount of adsorption to the film performed the same actuation as the transmissometry of albumin, the physiological saline washed it for 1 minute. Next, it computed as the protein amount of adsorption per film weight by carrying out beating of the hollow filament-like film to 5mm spacing extent, and carrying out the quantum of the plasma protein stirred and extracted in the physiological saline which contains lauryl acid sodium 1.0%. Protein concentration used BCA protein assay (made in Pierce). In addition, it compared with a specimen and coincidence using the film (what was obtained by being immersed in ethanol for one day after the film of the example 1 in front of gamma irradiation was immersed in the sodium hypochlorite with an available chlorine concentration of 1,500 ppm for two days) which does not contain PVP as positive control.

[0055]

[Example 1] (Film production and clearance of a residual solvent) It dissolved in 77.7 % of the weight of N,N-dimethylacetamide, and 18.0 % of the weight (product P-1700 made from Amoco Engineering Polymers) of polysulfones and 4.3 % of the weight (BASF A.G. make K90, weight average molecular weight 1,200,000) of polyvinyl pyrrolidones were used as the uniform solution. Here, the mixing ratio of the polyvinyl pyrrolidone to the polysulfone in a film production undiluted solution was 23.9 % of the weight. This film production undiluted solution was kept at 60 degrees C, and it was immersed to the coagulation bath which is made to breathe out from a spinning port (double annular nozzle 0.1mm - 0.2 mm to 0.3 mm), is made to pass a 0.96m air gap, and consists of 75-degree C water with the internal liquid which consists of a mixed solution of 30 % of the weight of N,N-dimethylacetamide, and 70 % of the weight of water. At this time, from a spinning port to the coagulation bath was surrounded by the cylinder-like cylinder, the humidity in a cylinder was controlled and temperature was controlled for the nitrogen gas which contained the steam in the cylinder at 51 degrees C 54.5% with the sink. Spinning speed was fixed to a part for 80m/. Here, the ratio of the air gap to spinning speed was 0.012m/(a part for m/). The residual solvent in the film was removed after cutting the rolled-round thread by washing a 80-degree C hot water shower over 2 hours from the cutting plane upper part of a thread (die length of 30cm, 9400 film numbers).

[0056] The equipment shown in drawing 1 is used. (Desiccation of the humid film and insolubilization processing of PVP) The thread after the above-mentioned residual solvent clearance (the water content of the film of a thread core 300% 300%) [water content] The difference of the water content of the film [in / in the water content of the film of the thread periphery section / the core and the periphery section of a thread] has arranged each uniformly by regular intervals 300% by setting a thread to a tray for 90 bundles 0% in a microwave irradiation reactor (3m [/second] wind speed in an irradiation reactor). It fixed with the fixture so that the cutting plane of a thread might surely become a top or the bottom at this time. Furthermore, six waveguides were uniformly fixed by regular intervals, respectively so that microwave might be irradiated by each thread in an irradiation reactor at homogeneity.

[0057] The microwave exposure was carried out for 18 minutes with the microwave output of 30kW (kilowatt) to this thread. The water content of the thread located in the core in an irradiation reactor at this event was 42% (for the water content of the film of a thread core, the water content of the film of 44% and the thread periphery section is 40%). Water content obtained less than 1% of desiccation film (thread) by reducing only the output of microwave to 21kW succeedingly, and carrying out a microwave exposure for 8 more minutes.
[0058] Moreover, the following actuation was performed between the time of desiccation initiation, and the time of desiccation termination.
(1) Water was poured in piping made from a nonmetal installed in the surroundings of the tray in an irradiation reactor.
(2) It was made to rotate at the rate of 4 revolutions of a tray in 1 minute.
(3) The temperature in an irradiation reactor was held at 70**2 degrees C.
(4) Dehumidification air (10% or less of humidity) was ventilated from the lower part of each thread from the lower part of a thread to the upper part at the 4m [/second] wind speed. At this time, the 0.4m [/second] wind speed was measured by the thread average from the upper part of a thread at the time of desiccation initiation. Furthermore, a part of PVP in the film was insolubilized by irradiating the gamma ray of 2.5Mrad(s) at the obtained desiccation film (thread).
[0059] (Performance-evaluation result) Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all threads are shown in a table 1. When the thread (film) equivalent to an average value was used as the module of 2 the effective filtration area of 1.5m and path clearance of beta 2-microglobulin was surveyed, it turned out that it is by part for 32mL/, and it became clear that it is equivalent to a part for path clearance 32.5mL/computed by having substituted it for the formula (5). Furthermore, when this module performed transit measurement of a urea and vitamin B12, the path clearance and the permeability of a urea were part 83% for 185mL(s)/, respectively. Moreover, about vitamin B12, it was part 48% for 95mL(s)/similarly. Measurement is [0044]. It carried out by the same approach. Moreover, 62% of the total amount of PVP in the film was insoluble in water. As a result of carrying out a membranous eluting material test, the absorbance of effluent test fluid was 0.04 or less. Moreover, since the pit hold-back agent was not used, in effluent test fluid, the pit hold-back agent was contained and was not. Furthermore, as for this film, compared with the positive control film, the amount of platelet adhesion became low (positive control film 43 Unit/m2) clear [that the amount of adhesion of plasma protein is also low] (positive control film 63 mg/g). It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet from the engine performance mentioned above. Moreover, since the transmission of albumin was excellent also in the path clearance of beta 2-microglobulin few, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.
[0060]
[Example 2] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 78 % of the weight 4% of the weight. The mixing ratio of the polyvinyl

pyrrolidone to the polysulfone in the film production undiluted solution at this time was 22.2 % of the weight. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 1. It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet. Moreover, there was little transmission of albumin, and since excelling also in the path clearance of beta 2-microglobulin was suggested, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0061]

[Example 3] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 77.2 % of the weight 4.8% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 26.7 % of the weight. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 1. It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet. Moreover, there was little transmission of albumin, and since excelling also in the path clearance of beta 2-microglobulin was suggested, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0062]

[Example 4] The same actuation as an example 3 was performed except having used the mixing solution which turns into internal liquid from 52 % of the weight of N,N-dimethylacetamide, and 48 % of the weight of water. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 1. It became clear that this film has very few elution volumes from the film, and there is little adhesion of blood protein and a platelet. Moreover, there was little transmission of albumin, and since excelling also in the path clearance of beta 2-microglobulin was suggested, it turned out that it is the film excellent also in the dialysis engine performance. Furthermore, it became clear that there are also few engine-performance differences with the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of all threads compared with the example 1 of a comparison.

[0063]

[The example 1 of a comparison] The same actuation as an example 1 was performed except there being nothing gamma ray Teru putting. This result is shown in a table 2. It became clear that the absorbance of elution test liquid exceeds 0.04 for elution of PVP. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0064]

[The example 2 of a comparison] The same actuation as an example 1 was performed except

having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 77.0 % of the weight 5.0% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 27.8 % of the weight. The engine performance of this thread is shown in a table 2. Since the mixing ratio of the polyvinyl pyrrolidone to the polysulfone in a film production undiluted solution is over 27 % of the weight, an elution volume and film internal-surface PVP concentration are increasing. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0065]

[The example 3 of a comparison] The same actuation as an example 1 was performed except having made the polyvinyl pyrrolidone in a film production undiluted solution, and having made N,N-dimethylacetamide into 78.4 % of the weight 3.6% of the weight. The mixing ratio of the polyvinyl pyrrolidone to the polysulfone in the film production undiluted solution at this time was 20.0 % of the weight. The engine performance of this thread is shown in a table 2. It became clear that the amount of PVP of a film internal surface is less than 30%. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0066]

[The example 4 of a comparison] The same actuation as an example 3 was performed except having used the mixing solution which turns into internal liquid from 60 % of the weight of N,N-dimethylacetamide, and 40 % of the weight of water. The engine performance of this thread is shown in a table 2. This film was engine performance for which the permeability of albumin is over 0.3%, and the permeability of PVP also exceeds 75%. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0067]

[The example 5 of a comparison] The same actuation as an example 1 was performed except having used the mixing solution which turns into internal liquid from 10 % of the weight of N,N-dimethylacetamide, and 90 % of the weight of water. The engine performance of this thread is shown in a table 2. The amount of water penetration of pure water was the engine performance which is less than 10mL(s)/(m2 and hr-mmHg). The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0068]

[The example 6 of a comparison] The same actuation as an example 1 was performed except having made drying temperature into 170 degrees C. The engine performance of this thread is shown in a table 2. All PVP in the film of this film was insoluble in water. This film is used as the module of 2 the effective filtration area of 1.5m, and it is [0044]. When it was alike and clinical blood assessment was carried out by the shown approach, the leuco PENIA symptom that a dialysis patient's white blood cell count fell temporarily was observed. The performance evaluation performed only the thread located in the core in an irradiation reactor.

[0069]

[The example 7 of a comparison] The same actuation as an example 1 was performed except not pouring water in piping made from the nonmetal installed in the surroundings of the tray in an irradiation reactor, and the tray lower part. Each physical properties of the thread (thread of the outermost engine performance) which has the value from which it separated most to the average and this average of each physical properties when evaluating all the threads at this time are shown in a table 3. Discharge was observed from the metal member of the tray between microwave exposures. In the thread which exists on the outskirts of a metal fixture of a tray with

this discharge and heating, that whose amount of water penetration is 0 (zero) was seen, and it became clear that the thread of the poor engine performance is generated clearly.

[0070]

[A table 1]

	実施例1		実施例2		実施例3		実施例4	
	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能の糸束の値
膜内径(μm)	195	195	200	200	195	195	195	195
膜外径(μm)	285	286	286	290	285	283	285	289
透水量(mL/(m²·hr·mmHg))	22	19	18	15	23	20	420	400
アルブミンの透過率（%）	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下
PVPの透過率（%）	4	4	4	4	5	5	72	72
膜内表面PVP濃度(重量%)	35	35	30	30	44	44	36	36
水に不溶であるPVPの有無	有り	有り	有り	有り	有り	有り	有り	有り
溶出物試験液の吸光度	0.022	0.022	0.020	0.020	0.035	0.035	0.022	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し	無し	無し	無し	無し	無し	無し
血小板粘着量(LDH-Unit/m²)	15.6	15.7	17.7	17.5	4.1	4.1	14.0	14.1
血漿タンパク質吸着量（mg/g）	2.2	2.2	5.5	5.6	1.9	1.9	2.0	2.0
乾燥前湿潤膜の透水量(mL/(m²·hr·mmHg))	190	190	170	170	260	260	3100	3100
乾燥前湿潤膜のアルブミンの透過率（%）	0.32	0.32	0.34	0.34	0.35	0.35	0.51	0.51
乾燥前湿潤膜のPVPの透過率（%）	77	77	84	84	84	84	99	99

[0071]

[A table 2]

	比較例1	比較例2	比較例3	比較例4	比較例5	比較例6
膜内径(μm)	195	201	200	196	202	190
膜外径(μm)	282	291	292	295	291	281
透水量(mL/m²・hr・mmHg)	22	35	16	960	9	15
アルブミンの透過率（%）	0.01以下	0.01以下	0.01以下	0.37	0.01以下	0.01以下
PVPの透過率（%）	4	5	4	79	0	4
膜内表面PVP濃度(重量%)	35	46	28	33	34	36
水に不溶であるPVPの有無	無し	有り	有り	有り	有り	有り
溶出物試験液の吸光度	0.047	0.088	0.016	0.020	0.020	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し	無し	無し	無し	無し
血小板粘着量(LDH-Unit/m²)	15.5	3.8	19.2	15.4	15.1	16.6
血漿タンパク質吸着量（mg/g）	2.1	2.1	6.0	2.8	2.1	3.0
乾燥前湿潤膜の透水量(mL/m²・hr・mmHg)	190	310	130	8500	76	190
乾燥前湿潤膜のアルブミンの透過率（%）	0.32	0.38	0.32	0.60	0.17	0.31
乾燥前湿潤膜のPVPの透過率（%）	77	85	76	100	52	76

[0072]
[A table 3]

	比較例7	
	全糸寒の平均値	最外性筒の糸寒の値
膜内径(μm)	195	191
膜外径(μm)	235	230
透水量(mL/(m²·hr·mmHg))	16	0
アルブミンの透過率 (%)	0.01以下	測定不可能
PVPの透過率 (%)	3	測定不可能
膜内表面 PVP 濃度(重量%)	35	35
水に不溶であるPVPの有無	有り	有り
溶出物試験液の吸光度	0.022	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し
血小板粘着量 (LDH-Unit/m²)	15.0	測定不可能
血漿タンパク質吸着量 (mg/g)	2.1	2.1
乾燥前湿潤膜の透水量(mL/(m²·hr·mmHg))	190	190
乾燥前湿潤膜のアルブミンの透過率 (%)	0.32	0.32
乾燥前湿潤膜のPVPの透過率 (%)	77	77

DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]

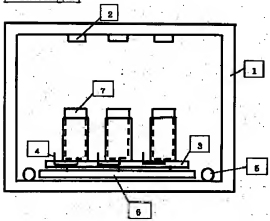
[Drawing 1] It is the front view showing an example of the manufacturing installation of the blood purification film of this invention.

[Description of Notations]

1 Container
2 Microwave Teru Gunner Stage
3 A Means to Fix, and to Carry in and Take Out Thread
4 Ventilation Means
5 Liquid Passage Means
6 Revolution Means
7 Thread

DRAWINGS

[Drawing 1]



[Translation done.]

(19)日本国特許庁（ＪＰ）　(12)公開特許公報（Ａ）　(11)特許出願公開番号
特開2003－284931
(P2003－284931A)
(43)公開日　平成15年10月７日(2003.10.7)

(51)Int.Cl.'	識別記号	ＦＩ		テーマコード'(参考)
Ｂ０１Ｄ　69/08		Ｂ０１Ｄ　69/08		３Ｌ１１３
Ａ６１Ｍ　1/18	５００	Ａ６１Ｍ　1/18	５００	４Ｃ０７７
Ｆ２６Ｂ　3/347		Ｆ２６Ｂ　3/347		４Ｄ００６
25/00		25/00	Ａ	

審査請求　未請求　請求項の数10　ＯＬ　（全 12 頁）

(21)出願番号　特願2002－87779(P2002－87779)
(22)出願日　平成14年３月27日(2002.3.27)

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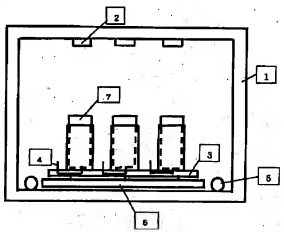
最終頁に続く

(54)【発明の名称】　中空糸膜の乾燥装置

(57)【要約】
【課題】　糸束状に製束された湿潤膜をマイクロ波照射により複数束同時に乾燥するための装置において、全ての糸束を均一に乾燥できる装置を提供する。
【解決手段】　容器内に、マイクロ波照射手段と、糸束を固定し搬入・搬出する手段と、誘電体損失係数が１～５０である液体を通過させる手段とを有することを特徴とする中空糸膜の乾燥装置。



【特許請求の範囲】

【請求項１】　糸束状に製束された湿潤膜を乾燥するための装置であって、容器内にマイクロ波照射手段と、糸束状に製束された湿潤膜を固定し搬入・搬出する手段と、容器内に誘電損失係数が１～５０である液体を通過させる手段とを有することを特徴とする中空糸膜の乾燥装置。

【請求項２】　容器内の金属部位あるいは金属部位の周辺に誘電損失係数が１～５０である液体を通過させるための配管を有することを特徴とする請求項１記載の装置。

【請求項３】　マイクロ波照射手段が複数存在することを特徴とする請求項１または２に記載の装置。

【請求項４】　糸束に通風する手段を有することを特徴とする請求項１～３のいずれかに記載の装置。

【請求項５】　糸束状に製束された湿潤膜を固定し搬入・搬出する手段を回転させる手段をさらに有することを特徴とする請求項１～４のいずれかに記載の装置。

【請求項６】　容器がマイクロ波遮断機能を有することを特徴とする請求項１～５のいずれかに記載の装置。

【請求項７】　容器内の温度を一定に保つ温度制御手段をさらに有することを特徴とする請求項１～６のいずれかに記載の装置。

【請求項８】　容器内の気体を循環する手段をさらに有することを特徴とする請求項１～７のいずれかに記載の装置。

【請求項９】　容器内の気体を外部の気体と置換する手段をさらに有することを特徴とする請求項１～８のいずれかに記載の装置。

【請求項１０】　中空糸膜が中空糸状血液浄化膜である請求項１～９のいずれかに記載の装置。

【発明の詳細な説明】

【０００１】

【発明の属する技術分野】本発明は、中空糸膜の乾燥装置に関するものである。より詳細には、本発明は、糸束状に製束された湿潤膜をマイクロ波照射により複数束同時に乾燥するための装置であって、照射炉内の局所的な温度上昇による一部の糸束の性能不良を防ぎ、且つ全ての糸束を均一に乾燥することを目的とした乾燥装置に関する。

【０００２】

【従来の技術】近年、選択的な透過性を有する膜を利用する技術がめざましく進歩し、これまでに気体や液体の分離フィルター、医療分野における血液透析器、血液濾過器、血液成分選択分離フィルター等の広範な分野での実用化が進んでいる。膜膜の材料としては、セルロース系（再生セルロース系、酢酸セルロース系、化学変性セルロース系等）、ポリアクリロニトリル系、ポリメチルメタクリレート系、ポリスルホン系、ポリエチレンビニルアルコール系、ポリアミド系等のポリマーが用いられてきた。このうちポリスルホン系ポリマーは、その熱安定性、耐酸、耐アルカリ性に加え、製膜原液に親水化剤を添加して製膜することにより、血液適合性が向上することから、半透膜素材として注目され研究が進められてきた。

【０００３】一方、膜を接着してモジュールを作製するためには膜を乾燥させる必要があるが、有機高分子よりなる多孔膜、なかでもポリスルホン系等の疎水性ポリマーからなる透析膜、限外濾過膜は、製膜後に乾燥させると乾燥前に比べ著しく透水量が低下することが知られている。そのため膜は常に湿潤状態か、水に浸漬させた状態で取り扱う必要があった。

【０００４】この対策として従来からとられてきた方法は、製膜後、乾燥前にグリセリン等の低揮発性有機液体を多孔膜中の空孔部分に詰めておくことであった。しかしながら、低揮発性有機液体は、一般に高粘度なため、洗浄除去に時間がかかり、膜をモジュール成型して洗浄後も微量ではあるが低揮発性有機液体由来の溶出物等（低揮発性有機液体と化学反応して生成した様々な誘導体）がモジュール封入被中にみられることに問題があった。

【０００５】低揮発性有機液体を用いずに乾燥させる方法として、特開平６－２７７４７０号公報には、低揮発性有機液体の代わりに塩化カルシウム等の無機塩を用いる方法が示されているが、洗浄除去する必要性に変わりはない。また、微量であるとしても残存した無機塩が透析患者に与える悪影響が危惧される。

【０００６】また、膜の乾燥方法として、特開平１１－３３２９８０号公報には、中空糸膜に対し水蒸気による湿熱処理を行いながらマイクロ波を照射する中空糸膜の製造方法が示されている。しかし、乾燥でありながら膜の変形を防ぐために水蒸気処理しているとから乾燥時間を長くする欠点があり、さらに、グリセリン等の低揮発性有機液体を付着させてからの乾燥であることから、膜からの溶出物を低減させるという目的は達成されない。

【０００７】特開平８－５２３３１号公報及び特公平８－９６６８号公報には、低揮発性有機液体を用いずに乾燥処理をしたポリビニルピロリドンを含む親水化膜が開示されている。これらには、血液から血漿成分を分離する性能が記載されているが、血漿タンパクが透過することから透析膜としては有効でないことが分かる。また、ポリビニルピロリドンを分解・変性させる温度で乾燥していることから、膜からの溶出物を低減させるという目的においては極めて好ましくない製法である。

【０００８】また、特開平６－２９６８６号公報には血液が直接接触する膜内表面でのポリビニルピロリドンの存在率を２０～５０％程度にした中空糸膜が開示されている。これは主に血液タンパク、血小板等の付着物を少なくするための湿潤膜を示すものである。従って、血

液タンパクが付着しにくいことから濾液速度の経時変化が起こりにくいことが示されているが、アルブミンの透過性が低い等の透析性能についての記載は一切無い。

【０００９】本発明者は、特定の性能を有する湿潤膜をグリセリン等の低揮発性有機液体を含浸せずに乾燥して高性能な血液浄化膜を製造する方法を提案して特許出願した（特願２００１－２２２４６号）。しかし、その後の検討の結果、糸束状にして乾燥した場合、糸束の中心部と外周部の膜とでは若干の性能差が生じることが明らかとなった。

【００１０】そこで本発明者は、糸束内の性能差を改善した血液浄化膜を製造する方法を提案して特許出願した（特願２００１－３０９６７３号、特願２００１－３０９６７４号、特願２００１－３０９６７５号）。しかし、本発明者らのその後のさらなる検討の結果、複数の糸束を同時に乾燥するためにマイクロ波照射装置（照射炉）をスケールアップした場合には、これらの方法によっても、糸束の局所的な温度上昇が起こり、一部の糸束が性能不良となることが明らかとなった。

【００１１】

【発明が解決しようとする課題】本発明の課題は、糸束状に製束された湿潤膜をマイクロ波照射により複数同時に乾燥するための中空糸膜の乾燥装置であって、照射炉内の局所的な温度上昇による一部の糸束の性能不良を防ぎ、且つ全ての糸束を均一に乾燥することを目的とした乾燥装置を提供することにある。

【００１２】

【課題を解決するための手段】以上の如くモジュールからの溶出物の原因となる膜孔保持剤を用いずに乾燥した透析性能を有する血液浄化用乾燥膜は本発明者等の出願発明（特願２００１－２２２４６号）までなかった。その原因は、膜孔保持剤を用いずに乾燥させると、湿潤状態とは全く異なった低性能の膜となることであった。そこで、本発明者等は、前期出願により、あらかじめ目標とする性能よりも高透水量で大孔径である特定の性能を有する湿潤膜を作製しておき、これを乾燥・収縮させて目標の透析性能を有する膜を製造するというこれまでにない、誰も思いつかなかった発想に基づき鋭意研究を進めた結果、溶出物が極めて少なく、血液タンパクや血小板の付着が少ない選択透過性に優れた透析性能を有する膜を得る方法を提供した。

【００１３】その後、さらに研究を進めたところ、本発明者らは、特願２００１－２２２４６号の方法によって血液浄化膜を製造する際、湿潤膜を糸束状にして乾燥すると、糸束の中心部と外周部の膜とでは、透水量や透過性能にばらつきが生じることを発見した。そこで、ばらつきをなくすために鋭意研究した結果、乾燥工程を工夫することで、ばらつきが抑えられることを見出し新たに特許出願した（特願２００１－３０９６７３号、特願２００１－３０９６７４号、特願２００１－３０９６７５号）。

【００１４】ところが、その後の検討の結果、複数の糸束を同時に乾燥するためにマイクロ波照射装置をスケールアップした結果、性能不良となる糸束が発生した。原因は明確ではないが、スケールアップにより糸束を固定するために用いられるトレーを構成している金属部材が加熱・放電することによって照射炉内の糸束の一部が急速に温度上昇し、性能不良となることが推測される。トレーは、照射炉内への糸束の出し入れにも用いられるため、金属を用いずに、例えばプラスチックのみで作製することは、機械的強度が低下するために困難である。そこで、金属部材の加熱・放電を防ぐために鋭意研究した結果、糸束中の水分子の振動（水分子の加熱）に用いられる以外の余剰なマイクロ波を効率良く除去する流体（液体）を照射炉内、特に金属部材あるいはその周辺に通過させることで糸束の一部の局所的な温度上昇を抑えられることを見出し本発明に至ったものである。

【００１５】すなわち本発明は、（１）糸束状に製束された湿潤膜を乾燥するための装置であって、容器内にマイクロ波照射手段と、糸束状に製束された湿潤膜を固定し搬入・搬出する手段と、容器内に誘電損失係数が１～５０である液体を通過させる手段とを有することを特徴とする中空糸膜の乾燥装置、（２）容器内の金属部位あるいは金属部位の周辺に誘電損失係数が１～５０である液体を通過させるための配管を有することを特徴とする上記（１）記載の装置、（３）マイクロ波を照射する手段が複数存在することを特徴とする上記（１）または（２）に記載の製造装置、（４）糸束に通風する手段を有することを特徴とする（１）～（３）のいずれかに記載の製造装置、（５）糸束を固定し出し入れするために用いられる手段を固定して、さらに回転させる手段を有することを特徴とする（１）～（４）のいずれかに記載の製造装置、（６）容器がマイクロ波を遮断する機能を有することを特徴とする（１）～（５）のいずれかに記載の製造装置、（７）容器が容器内の気体の温度を一定に保つ機能を有することを特徴とする（１）～（６）のいずれかに記載の製造装置、（８）容器が容器内の気体を循環する機能を有することを特徴とする（１）～（７）のいずれかに記載の製造装置、（９）容器が容器内の気体を外部の気体と入れ換える機能を有することを特徴とする（１）～（８）のいずれかに記載の製造装置、及び（１０）中空糸膜が中空糸状血液浄化膜である上記（１）～（９）のいずれかに記載の装置、に関するものである。

【００１６】

【発明の実施の形態】本発明は、中空糸状血液浄化膜の乾燥装置に限られるわけではないが、以下には、本発明の中空糸状血液浄化膜（以下単に「膜」又は「中空糸状膜」ともいう）の乾燥装置について説明する。本発明の乾燥装置を用いて製造される中空糸状血液浄化膜は、膜

孔保持剤を含まないことが好ましいが、それに限られるわけではない。

【００１７】以下には、本発明の乾燥装置を用いて乾燥される中空糸状血液浄化膜の製造方法をまず説明する。本発明の中空糸状血液浄化膜の製造方法は、高透水量で大きな孔径の湿潤膜をあらかじめ製造しておき、脱溶剤後に膜孔保持剤を含浸させずに乾燥させることに特徴を有する。

【００１８】通常、中空糸状血液浄化膜を製造する際に用いられる膜孔保持剤には、粘性を有する有機物と人体への毒性が懸念される無機物に分類される。粘性を有する有機物からなる膜孔保持剤は、粘性が高いために完全に洗浄除去することが困難であることから、膜中に残存して膜からの溶出量を増加させ、さらに残存した膜孔保持剤と化学反応して有害物を生じる原因と成り得る。一方、無機物からなる膜孔保持剤においても、微量に残存するため透析患者に与える悪影響が危惧される。

【００１９】本発明でいう膜孔保持剤とは、乾燥時の性能低下を防ぐために乾燥前までの製造過程で膜中の空孔部分に詰めておく物質である。膜孔保持剤を含んだ溶液に湿潤膜を浸漬することによって膜中の空孔部分に膜保持剤を詰めることが可能である。乾燥後も膜孔保持剤を洗浄・除去さえすれば、膜孔保持剤の効果により湿潤膜と同等の透水量、阻止率等の性能を保持することが可能である。

【００２０】膜孔保持剤としては、エチレングリコール、プロピレングリコール、トリメチレングリコール、１，２－ブチレングリコール、１，３－ブチレングリコール、及び蔗糖脂肪酸エステル等の有機化合物および塩化カルシウム、炭酸ナトリウム、酢酸ナトリウム、硫酸マグネシウム、硫酸ナトリウム、塩化亜鉛等の無機塩を挙げることができる。

【００２１】また、本発明において、高透水量で大きな孔径の湿潤膜とは、透水量が１００mL／（m²・hr・mmHg）以上であって、重量平均分子量４０，０００のポリビニルピロリドンの透過率が７５％を超え、且つ牛血漿系におけるアルブミンの透過率が０．３％以上である性能を有する湿潤膜を意味する。

【００２２】牛血漿アルブミンの透過率は、以下のような方法で測定することが可能である。まず、長さ２０cmの中空糸状膜を１００本束ねて小型モジュールを作製する。このモジュールに３７℃に加温したヘパリン添加牛血漿（ヘパリン５０００ＩＵ／l、タンパク濃度６．０g／dL（デシリットル））を膜内表面側に線速１．０cm／秒で通過させ、モジュールの入り圧と出圧の平均圧力５０mmHgにて３０分間限外濾過を行なう。得られた濾液と元液の濃度の測定は、紫外分光光度計により２８０nmの波長にて測定し、下記の式（１）に代入して透過率を算出する。

$$\text{透過率}(\%) = (\text{濾液の吸光度}) \times 100 / (\text{元液の吸光度}) \quad (1)$$

【００２３】ポリビニルピロリドンの透過率は、濾過する水溶液を３重量％のポリビニルピロリドン（ＢＡＳＦ社製　Ｋ３０、重量平均分子量４０，０００）のリン酸バッファー（０．１５mol／リットル、pH７．４）水溶液にして、モジュールの入り圧と出圧の平均圧力を２００mmHgにした以外は、牛血漿アルブミンの透過率の測定と同様な操作を行うことにより求められる。

【００２４】高透水量で大きな孔径の湿潤膜は、ポリスルホン系ポリマー（以下単に「ポリマー」ともいう）、ポリビニルピロリドン、及び溶剤からなる製膜原液を、内部液とともに２重環状ノズルから吐出させ、エアギャップを通過させた後、凝固浴で凝固させる製造方法において、内部液にポリマーの溶剤の水溶液を用いることにより製造可能である。

【００２５】内部液は、膜の中空部と内表面を形成させるものであるが、内表面の孔径は、内部液中の溶剤濃度に比例して大きくなることが判っている。本発明では、湿潤膜を乾燥収縮させることにより目標の性能の透析膜が得られることから、内部液中の溶剤濃度を、目標とする透析性能を有する湿潤膜を製造する時に比べて、高濃度にする必要がある。

【００２６】本発明で用いられるポリスルホン系ポリマーとしては、下記の式（２）、または式（３）で示される繰り返し単位を有するものが挙げられる。なお、式中のＡｒはパラ位での２置換のフェニル基を示し、重合度や分子量については特に限定しない。

$$-O-Ar-C(CH_3)_2-Ar-O-Ar-SO_2-Ar- \quad (2)$$

$$-O-Ar-SO_2-Ar- \quad (3)$$

【００２７】ポリビニルピロリドンは高分子量のものほど膜への親水化効果が高いため、高分子量のものほど少量で十分な効果が発揮できることから、本発明においては重量平均分子量９００，０００以上のポリビニルピロリドンが使用される。９００，０００より小さい重量平均分子量を有するポリビニルピロリドンを用いて膜への親水化効果を付与するためには大量のポリビニルピロリドンを膜中に残存させる必要があるが、このために膜からの溶出物が増加することになる。また、逆に溶出物を下げるために９００，０００よりも小さい重量平均分子量のポリビニルピロリドンの膜中での残存量を少なくすると親水化効果が不十分となってしまい、その結果血液透析を行ったとき濾過速度の経時的低下をきたし十分な効果を発揮できない。

【００２８】また、ポリスルホン系ポリマーとポリビニルピロリドンの溶解に用いられる溶剤は、これら両方を共に溶解するものであり、Ｎ－メチル－２－ピロリドン、Ｎ，Ｎ－ジメチルホルムアミド、Ｎ，Ｎ－ジメチル

アセトアミド等である。

【００２９】製膜原液中のポリマー濃度は、製膜可能で、かつ得られた膜が膜としての性能を有するような濃度の範囲であれば特に制限されず、５～３５重量%、好ましくは１０～３０重量%である。高い透水性能を達成するためには、ポリマー濃度は低い方がよく、１０～２５重量%が好ましい。

【００３０】さらに重要なことはポリビニルピロリドンの添加量であり、ポリマーに対するポリビニルピロリドンの混和比率が２７重量%以下、好ましくは１０～２７重量%、さらに好ましくは２０～２７重量%である。ポリマーに対するポリビニルピロリドンの混和比率が２７重量%を超えると溶出量が増える傾向にあり、また１０重量%未満では製膜原液の粘性が低いためにスポンジ構造の膜を得ることが困難である。また、原液粘度、溶解状態を制御する目的で、水、貧溶剤等の第４成分を添加することも可能であり、その種類、添加量は組み合わせにより随時行なえばよい。

【００３１】凝固浴としては、例えば水；メタノール、エタノール等のアルコール類；エーテル類；ｎ－ヘキサン、ｎ－ヘプタン等の脂肪族炭化水素類などポリマーを溶解しない液体が用いられるが、水が好ましい。また、凝固浴にポリマーを溶解する溶剤を若干添加することにより凝固速度をコントロールすることも可能である。凝固浴の温度は、－３０～９０℃、好ましくは０～９０℃、さらに好ましくは０～８０℃である。凝固浴の温度が９０℃を超えたり、－３０℃未満であると、凝固浴中の中空糸膜の表面状態が安定しにくい。

【００３２】脱溶剤洗浄後の乾燥は、中空糸状膜を多数さらに、糸束の中心部と外周部の乾燥速度の差をなくすために、糸束内には４０℃を超えない温度の除湿気体を通風することが好ましい。糸束内に通風するとは中空糸状膜間に風を流すことを意味する。本発明において、４０℃以上１２０℃以下の温度の除湿気体を糸束内に通風することは、糸束内に通風すると同時に糸束に対し加熱乾燥を行なっていることを意味する。

【００３６】本発明において、糸束へのマイクロ波照射は、密閉された照射炉内（容器内）で複数束同時に行なわれる。糸束は金属部材と非金属（例えばプラスチック）からなるトレー上に固定させる。マイクロ波は糸束中の水分子の振動（水分子の加熱）に消費させるが、一方で余剰のマイクロ波は金属部材の加熱・放電の原因となる。この加熱・放電が糸束の局所的な温度上昇を引き起こし、糸束の一部の性能不良の原因となる。性能不良を無くすために、本発明ではマイクロ波の吸収力の高い液体を照射炉内設置した配管内に流すことによって余剰のマイクロ波を取り除くことを可能とした。

【００３７】マイクロ波の吸収力は誘電損失係数の大きさに比例することから、誘電損失係数の大きな液体を流本束ねた糸束の形態（以後、単に『糸束』と呼ぶ）にて、十分に濡潤している糸束にマイクロ波照射することにより行なわれる。しかしながら、マイクロ波照射は低含水率の糸束をより均一に乾燥するのに適していることから、過加熱による膜の変形・溶融を防ぐために、糸束の平均含水率が２０～７０%、より好ましくは５０～７０%になる時点でマイクロ波照射の出力を低下させるのが好ましい。

【００３３】さらに、糸束の平均含水率が２０～７０%、好ましくは５０～７０%になる時点での膜糸束の中心部と外周部における膜の含水率の差が５%以内であることが、性能のばらつきを抑えるために好ましい。乾燥の時、糸束内に通風を行なうことによって、糸束の中心部と外周部における膜の含水率の差を５%以内にすることが可能である。ここで、糸束の中心部とは、糸束の円形状断面において中心点から直径の１／６の範囲をいう。また、糸束の外周部とは、糸束の円形状断面において外周から直径の１／６の範囲をいう。

【００３４】また、同様な理由から、乾燥開始時における糸束についても、糸束の中心部と外周部における膜の含水率の差が１０%以内であることが好ましい。脱溶剤後糸束を放置しておくと、糸束の中心部と外周部の含水率には差が生じるために、乾燥工程に入る直前に糸束を再度水中に浸漬することにより糸束中心部と外周部の含水率の差を１０%以内にすることが可能である。

【００３５】ここで、含水率とは、乾燥前の糸束（又は膜）の重量（Ａ（ｇ））と乾燥糸束（又は膜）の重量（Ｂ（ｇ））から（４）式により計算で求められるものをいう。

$$含水率\ (\%) = (A-B) \times 100 / B \qquad (4)$$

すことが好ましく、誘電損失係数の値が１～５０である液体であることが好ましい。誘電損失係数が１未満ではマイクロ波の吸収力が低いために好ましくなく、５０を超える液体は過冷却状態の水等であり、実用的でない。

【００３８】本発明における誘電損失係数とは、２，４５０ＭＨｚ（メガヘルツ）の周波数で測定された物質の比誘電率と誘電正接の値の積を意味する。誘電損失係数が１～５０の液体としては、水；メチルアルコール、エチルアルコール等のアルコール類；エチレングリコール、プロピレングリコール、トリメチレングリコール、１，２－ブチレングリコール、１，３－ブチレングリコール、２－ブテン－１，４－ジオール、２－メチル－２，４－ペンタジオール、２－エチル－１，３－ヘキサンジオール、グリセリン、テトラエチレングリコール、ポリエチレングリコール２００、ポリエチレングリコール３００、ポリエチレングリコール４００等のグリコール系又はグリセロール系化合物を挙げることができるが水が最も好ましい。

【００３９】本発明において導波管とはマイクロ波の照射源を意味する。導波管は糸束の数に比例して複数用い

ることが好ましい。また、マイクロ波の出力は高いことが好ましいが、乾燥させる膜の量及び含水率により最適値は異なる。

【００４０】乾燥後の膜に電子線及びγ線等の放射線を照射することにより、膜中のＰＶＰの一部を水に不溶化できることから、膜からの溶出量をより低減することが可能である。放射線の照射は、モジュール化前又はモジュール化後のどちらでも良い。また、膜中の全ＰＶＰを不溶化してしまうと、溶出量を低減できる一方で、透析時にロイコペニア症状が観察されることから好ましくない。

【００４１】本発明でいう水に不要であるＰＶＰとは、膜中の全ＰＶＰ量から水に可溶であるＰＶＰ量を差し引いたものである。膜中の全ＰＶＰ量は、窒素及びイオウの元素分析により容易に算出することができる。また、水に可溶であるＰＶＰ量は、以下の方法により求めることができる。膜をＮ－メチル－２－ピロリドンで完全に溶解した後、得られたポリマー溶液に水を添加してポリスルホン系ポリマーを完全に沈殿させる。さらに該ポリマー溶液を静置した後、上澄み液中のＰＶＰ量を液体クロマトグラフィーで定量することにより水に可溶であるＰＶＰを定量することができる。

【００４２】本発明の乾燥装置は、特に、糸束状に製束された膜孔保持剤を含まない湿潤膜を複数同時に乾燥するのに適する装置であって、本装置を用いて得られた膜

$$B\ (mL/分) = 0.636A + 29.99 \qquad (5)$$

ここで、β２－ミクログロブリンのクリアランスは、１．５m^2の有効膜面積のモジュールに、血液流量２００ｍL／分（膜内表面側）、透析液流量５００ｍL／分（膜外表面側）の条件下で日本人工臓器学会の性能評価基準に従い透析測定したものである。β２－ミクログロブリンのクリアランスは、透析患者の体力や病状及び病状の進行度に合わせて様々なものが要求されているが、ポリビニルピロリドンの透過率が７５％を超えるとアルブミンの透過率が０．３％を超えてしまうことから、ポリビニルピロリドンの透過率は７５％以下であることが必要である。

【００４５】また、本発明により作られた膜は、膜孔保持剤を製造工程で使用していないことから、膜孔保持剤由来の溶出物は存在しない。従って、本発明の膜の溶出物試験液の吸光度は０．０４未満であり、且つ該試験液中に膜孔保持剤を含まない。ここで、溶出物試験液とは、人工腎臓装置承認基準に基づき調整したものであり、２ｃｍに切断した乾燥中空糸状膜１．５ｇと注射用蒸留水１５０mLを日本薬局方の注射用ガラス容器試験のアルカリ溶出試験に適合するガラス容器に入れ、７０±５℃で１時間加温し、冷却後膜を取り除いた後蒸留水を加えて１５０mLとしたものを意味する。吸光度は２２０～３５０ｎｍでの最大吸収波長を示す波長にて紫外吸収スペクトルで測定する。人工腎臓装置承認基準では、膜孔保持剤を含まない乾燥膜であって、純水の透水量が１０～１，０００mL／（m^2・ｈｒ・ｍｍＨｇ）、重量平均分子量４０，０００のポリビニルピロリドンの透過率が７５％以下で、且つ牛血漿系におけるアルブミンの透過率が０．３％未満であり、さらにそれぞれの性能のバラツキが小さいことを特徴とする中空糸状血液浄化膜である。

【００４３】最近の血液透析療法では、透析アミロイド病状の改善のために原因物質とされているβ２－ミクログロブリン（分子量：１１，８００）を十分に透過させるが、アルブミン（分子量：６７，０００）はほとんど透過させない分画性を有する膜が求められており、本発明の膜は、牛血漿系におけるアルブミンの透過率が０．３％以下である。アルブミンの透過率が０．３％を超えることは体内に有効なアルブミンを大きく損失することを意味することから血液透析膜としては好ましくない。

【００４４】また、純水の透水量が１０mL／（m^2・ｈｒ・ｍｍＨｇ）以上の膜においては、ポリビニルピロリドンの透過率（Ａ（％））とβ２－ミクログロブリンのクリアランス（Ｂ（mL／分））とには下記の式（５）に示す一次関数的な相関関係が存在する。クリアランス評価には１．５m^2の有効膜面積を有する透析仕様のモジュールに成形・加工することが必要であるが、本評価方法では簡易的に測定可能であり、クリアランスを容易に推測することが可能である。

吸光度を０．１以下にすることが定められているが、本発明の膜は膜孔保持剤を保持しないことから０．０４未満を達成することが可能である。また、膜孔保持剤の有無については、該試験液を濃縮又は水分除去したものをガスクロマトグラフィー、液体クロマトグラフィー、示差屈折系、紫外分光光度計、赤外線吸光光度法、核磁気共鳴分光法、及び元素分析等の公知の方法により測定することにより検知可能である。また、膜中に膜孔保持剤を含むか否かについてもこれらの測定方法により検知可能である。

【００４６】本発明により作られた膜は、ポリスルホン系ポリマーとポリビニルピロリドンからなり、膜内表面におけるポリビニルピロリドンの濃度が３０～４５重量％である。膜の血液適合性に重要な因子は、血液が接する膜内表面の親水性であり、ポリビニルピロリドン（以下単に「ＰＶＰ」ともいう）を含有するポリスルホン系膜では、膜内表面のＰＶＰ濃度が重要である。膜内表面のＰＶＰ濃度が低すぎると膜内表面が疎水性を示し、血漿タンパク質が吸着しやすく、血液の凝固も起こりやすい。すなわち、膜の血液適合性不良となる。逆に膜内表面のＰＶＰ濃度が高すぎると、ＰＶＰの血液系への溶出量が増加し本発明の目的や用途にとっては好ましくない結果を与える。従って、本発明での膜内表面のＰＶＰの濃度は、３０～４０％の範囲であり、好ましくは３３～

４０％である。

【００４７】膜内表面のＰＶＰ濃度は、エックス線光量子スペクトル（Ｘ－ｒａｙ　Ｐｈｏｔｏｅｌｅｃｔｒｏｎ　ｓｐｅｃｔｒｏｓｃｏｐｙ、以下ＸＰＳ）によって決定される。すなわち、膜内表面のＸＰＳの測定は、試料を両面テープ上に並べた後、カッターで繊維軸方向に切開し、膜の内側が表になるように押し広げた後、通常の方法で測定する。すなわち、Ｃ１ｓ、Ｏ１ｓ、Ｎ１ｓ、Ｓ２ｐスペクトルの面積強度から、装置付属の相対感度係数を用いて窒素の表面濃度（窒素原子濃度）とイオウの表面濃度（イオウ原子濃度）から求めた濃度をいうものであり、ポリスルホン系ポリマーが（２）式の構造であるときには（６）式により計算で求めることができる。

$$\text{PVP濃度（重量\%）} = C_1M_1 \times 100 / (C_1M_1 + C_2M_2) \qquad (6)$$

ここで、C_1：窒素原子濃度（%）

C_2：イオウ原子濃度（%）

M_1：ＰＶＰの繰り返しユニットの分子量（１１１）

M_2：ポリスルホン系ポリマーの繰り返しユニットの分子量（４４２）

【００４８】次に本発明の乾燥装置の一例を、図面を参照して説明する。図１に示す乾燥装置は、容器（１）、マイクロ波照射手段（２）、糸束を固定し搬入・搬出する手段（３）、糸束通風手段（４）、誘電損失係数が１～５０である液体を通過させる手段（５）、及び、糸束を固定し搬入・搬出する手段（３）を固定して回転させる回転手段（６）からなる。

【００４９】糸束を固定し搬入・搬出するために用いられる手段（３）に固定された糸束（７）は、容器（１）内でマイクロ波照射手段（２）から照射されたマイクロ波により乾燥される。マイクロ波照射の間、通風手段（４）により除湿気体が糸束に流される。さらに容器内には、誘電損失係数が１～５０である液体を通過させる手段（５）が設けられているので、余剰なマイクロ波が吸収されて局所的な温度上昇が防止される結果、全ての糸束を均一に乾燥することができる。

【００５０】容器（１）は、さらに、（ａ）マイクロ波を遮断する機能、（ｂ）容器内の温度を一定に保つ温度制御手段、（ｃ）容器内の気体を循環する手段、及び（ｄ）容器内の気体を外部の気体と置換する手段を有する。マイクロ波を遮断する機能は、糸束の乾燥にマイクロ波を有効に使用するだけでなく、作業者の安全上必要である。また、乾燥バッチ間の性能差を無くすためには、容器内の温度を一定に保つことが必要である。さらに、容器内の気体を循環及び外部と入れ換えることにより、乾燥効率を向上することが可能である。

【００５１】マイクロ波照射手段（２）は、糸束（７）にマイクロ波を照射するために用いられるもので、形状、大きさは特に限定されないが、複数の糸束を均等に乾燥するためには、容器内に複数設置することが好ましい。糸束を固定し搬入・搬出するために用いられる手段（３）は、容器内での糸束の位置を固定して効率良く乾燥するために用いられるものである。さらに、固定・搬入・搬出手段（３）は、糸束の固定及び取り出しを容易にするために乾燥装置からの取り外しが可能である。糸束通風手段（４）は、糸束内に気体を通風するために用いられる。

【００５２】誘電損失係数が１～５０である液体を通過させる手段（５）は、液体を流すことができる手段であればどのようなものでも良いが、内部に誘電損失係数が１～５０である液体を通過させる非金属製の配管であることが好ましい。液体通過用の配管は、余剰のマイクロ波が、金属袖具などの金属部材を加熱・放電しやすいので、照射炉内の金属部材あるいはその周辺に設けることが好ましい。糸束を固定し搬入・搬出する手段（３）を固定して、さらに回転させる手段（６）は、糸束へのマイクロ波照射をより均等にするために用いられる。回転は水平方向である。

【００５３】

【実施例】以下にこの発明の実施例を示すが、本発明は、これに限定されるものではない。

（血小板粘着量の測定）膜への血小板粘着量の測定は、以下の操作手順で行った。長さ１５ｃｍの中空糸状膜を１０本束ねて小型モジュールを作製し、該モジュールにヘパリン添加ヒト新鮮血を線速１．０ｃｍ／秒にて１５分間通過させ、続いて生理食塩水を１分間通過させた。次に中空糸状膜を５ｍｍ間隔程度に細断し、０．５％ポリオキシエチレングリコールアルキルフェニルエーテル（和光純薬社製商品名トリトンＸ－１００）を含む生理食塩水中で超音波照射して膜表面に粘着した血小板から放出される乳酸脱水素酵素（以下、「ＬＤＨ」という）を定量することにより膜面積（内表面換算）当たりのＬＤＨ活性として算出した。酵素活性の測定はＬＤＨモノテストキット（ベーリンガー・マンハイム・山之内社製）を使用した。なお、陽性対照としてＰＶＰを含有しない膜（γ線照射前の実施例１の膜を有効塩素濃度１，５００ｐｐｍの次亜塩素酸ナトリウムに２日間浸漬した後、エタノールに１日間浸漬することにより得られたもの）を用い、試験品と同時に比較した。

【００５４】（血漿タンパク質吸着量）膜への血漿タンパク質吸着量は、限外濾過時間を２４０分にした以外はアルブミンの透過率測定と同様な操作を行った後、生理食塩水で１分間洗浄した。次に中空糸状膜を５ｍｍ間隔程度に細断し、１．０％ラウリル硫酸ナトリウムを含む生理食塩水中で撹拌して抽出した血漿タンパク質を定量することにより膜重量当たりのタンパク質吸着量として算出した。タンパク質濃度はＢＣＡプロテインアッセイ（ピアース社製）を使用した。なお、陽性対照としてＰＶＰを含有しない膜（γ線照射前の実施例１の膜を有効

塩素濃度１，５００ｐｐｍの次亜塩素酸ナトリウムに２日間浸漬した後、エタノールに１日間浸漬することにより得られたもの）を用い、試験品と同時に比較した。

【００５５】

【実施例１】（製膜及び残溶剤の除去）ポリスルホン（Ａｍｏｃｏ Ｅｎｇｉｎｅｅｒｉｎｇ Ｐｏｌｙｍｅｒｓ社製Ｐ－１７００）１８．０重量%、ポリビニルピロリドン（ＢＡＳＦ社製　Ｋ９０、重量平均分子量１，２００，０００）４．３重量%を、Ｎ，Ｎ－ジメチルアセトアミド７７．７重量%に溶解して均一な溶液とした。ここで、製膜原液中のポリスルホンに対するポリビニルピロリドンの混和比率は２３．９重量%であった。この製膜原液を６０℃に保ち、Ｎ，Ｎ－ジメチルアセトアミド３０重量%と水７０重量%の混合溶液からなる内部液とともに、紡口（２重環状ノズル　０．１ｍｍ－０．２ｍｍ－０．３ｍｍ）から吐出させ、０．９６ｍのエアギャップを通過させて７５℃の水からなる凝固浴へ浸漬した。この時、紡口から凝固浴までを円筒状の筒で囲み、筒の中に水蒸気を含んだ窒素ガスを流しながら、筒の中の湿度を５４．５%、温度を５１℃にコントロールした。紡速は、８０ｍ/分に固定した。ここで、紡速に対するエアギャップの比率は、０．０１２ｍ/（ｍ/分）であった。巻き取った糸束を切断後、糸束（長さ３０ｃｍ、膜本数９４００本）の切断面上方から８０℃の熱水シャワーを２時間かけて洗浄することにより膜中の残溶剤を除去した。

【００５６】（湿潤膜の乾燥及びＰＶＰの不溶化処理）図１に示す装置を用いて、上記の残溶剤除去後の糸束（含水率が３００%、糸束中心部の膜の含水率が３００%、糸束外周部の膜の含水率が３００%、糸束の中心部と外周部における膜の含水率の差が０%）９０束をマイクロ波照射炉（照射炉内の風速３ｍ/秒）内に、トレーに糸束をセットすることにより、それぞれを等間隔で均等に配置した。この時糸束の切断面が必ず上又は下になるように治具で固定した。さらに、照射炉内でそれぞれの糸束に均一にマイクロ波が照射されるように６本の導波管をそれぞれ等間隔で均等に固定した。

【００５７】該糸束に対してマイクロ波出力３０ｋＷ（キロワット）で１８分間マイクロ波照射した。この時点で照射炉内の中心部に位置する糸束の含水率は４２%（糸束中心部の膜の含水率が４４%、糸束外周部の膜の含水率が４０%）であった。引き続いてマイクロ波の出力のみを２１ｋＷに低下させてさらに８分間マイクロ波照射することにより含水率が１%未満の乾燥膜（糸束）を得た。

【００５８】また、乾燥開始時から乾燥終了時までの間、以下の操作を行なった。

（１）照射炉内のトレーの周りに設置した非金属製配管内に水を流した。

（２）トレーを１分間に４回転の速度で回転させた。

（３）照射炉内の温度を７０±２℃に保持した。

（４）各糸束の下部から４ｍ/秒の風速にて除湿空気（湿度１０%以下）を糸束の下部から上部へと通風した。この時、糸束の上部からは乾燥開始時において糸束平均で０．４ｍ/秒の風速が測定された。さらに、得られた乾燥膜（糸束）に２．５Ｍｒａｄのγ線を照射することにより膜中のＰＶＰの一部を不溶化した。

【００５９】（性能評価結果）全糸束を評価した時の各物性の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）の各物性を表１に示す。平均値に相当する糸束（膜）を有効濾過面積１．５m^2のモジュールにしてβ２－ミクログロブリンのクリアランスを実測したところ、３２ｍＬ/分で有ることが分かり、ＰＶＰの透過率を式（５）に代入して算出したクリアランス３２．５ｍＬ/分と同等であることが明らかとなった。さらに、該モジュールにて尿素、ビタミンＢ１２の透過測定を行ったところ、尿素のクリアランスと透過率はそれぞれ１８５ｍＬ/分、８３%であった。また、ビタミンＢ１２については同様に９５ｍＬ/分、４８%であった。測定は、

【００４４】と同様な方法で行った。また、膜中の全ＰＶＰ量の６２%が、水に不溶であった。膜の溶出物試験をした結果、溶出物試験液の吸光度は０．０４以下であった。また、膜孔保持剤を用いていないことから溶出物試験液中に膜孔保持剤は含まれて無かった。さらに、この膜は牛血清アルブミン吸着量が低く（牛血清アルブミン吸着量４３Ｕｎｉｔ/m^2）、且つ血漿タンパク質の粘着量も低いことが明らかとなった（牛血清アルブミン吸着量６３ｍｇ/ｇ）。以上に挙げた性能から、この膜は、膜からの溶出量が極めて少なく、血液タンパク質や血小板の付着が少ないことが明らかとなった。また、アルブミンの透過率が少なくβ２－ミクログロブリンのクリアランスにも優れることから透析性能にも優れた膜であることが分かった。さらに、全糸束の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）との性能差も比較例１に比べて少ないことが明らかとなった。

【００６０】

【実施例２】製膜原液中のポリビニルピロリドンを４重量%、Ｎ，Ｎ－ジメチルアセトアミドを７８重量%とした以外は、実施例１と同様な操作を行った。この時の製膜原液中のポリスルホンに対するポリビニルピロリドンの混和比率は２２．２重量%であった。この時の全糸束を評価した時の各物性の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）の各物性を表１に示す。この膜は、膜からの溶出量が極めて少なく、血液タンパク質や血小板の付着が少ないことが明らかとなった。また、アルブミンの透過率が少なく、且つβ２－ミクログロブリンのクリアランスにも優れることが示唆されたことから透析性能にも優れた膜であることが分かった。さらに、全糸束の平均値と該平均値に対して最

も外れた値を有する糸束（最外性能の糸束）との性能差も比較例１に比べて少ないことが明らかとなった。

【００６１】

【実施例３】製膜原液中のポリビニルピロリドンを４．８重量％、Ｎ，Ｎ－ジメチルアセトアミドを７７．２重量％とした以外は、実施例１と同様な操作を行った。この時の製膜原液中のポリスルホンに対するポリビニルピロリドンの混和比率は２６．７重量％であった。この時の全糸束を評価した時の各物性の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）の各物性を表１に示す。この膜は、膜からの溶出量が極めて少なく、血液タンパク質や血小板の付着が少ないことが明らかとなった。また、アルブミンの透過率が少なく、且つβ２－ミクログロブリンのクリアランスにも優れることが示唆されたことから透析性能にも優れた膜であることが分かった。さらに、全糸束の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）との性能差も比較例１に比べて少ないことが明らかとなった。

【００６２】

【実施例４】内部液にＮ，Ｎ－ジメチルアセトアミド５２重量％と水４８重量％からなる混和溶液を用いた以外は、実施例３と同様な操作を行った。この時の全糸束を評価した時の各物性の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）の各物性を表１に示す。この膜は、膜からの溶出量が極めて少なく、血液タンパク質や血小板の付着が少ないことが明らかとなった。また、アルブミンの透過率が少なく、且つβ２－ミクログロブリンのクリアランスにも優れることが示唆されたことから透析性能にも優れた膜であることが分かった。さらに、全糸束の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）との性能差も比較例１に比べて少ないことが明らかとなった。

【００６３】

【比較例１】γ線照射しない以外は、実施例１と同様な操作を行った。この結果を表２に示す。ＰＶＰの溶出のため溶出試験液の吸光度が０．０４を超えることが明らかとなった。性能評価は、照射炉内中心部に位置する糸束のみを行なった。

【００６４】

【比較例２】製膜原液中のポリビニルピロリドンを５．０重量％、Ｎ，Ｎ－ジメチルアセトアミドを７７．０重量％とした以外は、実施例１と同様な操作を行った。この時の製膜原液中のポリスルホンに対するポリビニルピロリドンの混和比率は２７．８重量％であった。この糸束の性能を表２に示す。製膜原液中のポリスルホンに対するポリビニルピロリドンの混和比率が２７重量％を超えているので、溶出量、膜内表面ＰＶＰ濃度が増加している。性能評価は、照射炉内中心部に位置する糸束のみを行なった。

【００６５】

【比較例３】製膜原液中のポリビニルピロリドンを３．６重量％、Ｎ，Ｎ－ジメチルアセトアミドを７８．４重量％とした以外は、実施例１と同様な操作を行った。この時の製膜原液中のポリスルホンに対するポリビニルピロリドンの混和比率は２０．０重量％であった。この糸束の性能を表２に示す。膜内表面のＰＶＰ量が３０％を下回っていることが明らかとなった。性能評価は、照射炉内中心部に位置する糸束のみを行なった。

【００６６】

【比較例４】内部液にＮ，Ｎ－ジメチルアセトアミド６０重量％と水４０重量％からなる混和溶液を用いた以外は、実施例３と同様な操作を行った。この糸束の性能を表２に示す。この膜は、アルブミンの透過率が０．３％を超えており、またＰＶＰの透過率も７５％を超える性能であった。性能評価は、照射炉内中心部に位置する糸束のみを行なった。

【００６７】

【比較例５】内部液にＮ，Ｎ－ジメチルアセトアミド１０重量％と水９０重量％からなる混和溶液を用いた以外は、実施例１と同様な操作を行った。この糸束の性能を表２に示す。純水の透水量が１０ｍＬ／（m^2・ｈｒ・ｍｍＨｇ）を下回る性能であった。性能評価は、照射炉内中心部に位置する糸束のみを行なった。

【００６８】

【比較例６】乾燥温度を１７０℃にした以外は、実施例１と同様な操作を行った。この糸束の性能を表２に示す。この膜は、膜中の全てのＰＶＰが水に不溶であった。この膜を有効濾過面積１．５m^2のモジュールにして

【００４４】に示した方法で臨床血液評価したところ、透析患者の白血球数が一時的に低下するロイコペニア症状が観察された。性能評価は、照射炉内中心部に位置する糸束のみを行なった。

【００６９】

【比較例７】照射炉内のトレーの周り及びトレー下部に設置した非金属製の配管内に水を流さない以外は実施例１と同様な操作を行った。この時の全糸束を評価した時の各物性の平均値と該平均値に対して最も外れた値を有する糸束（最外性能の糸束）の各物性を表３に示す。マイクロ波照射の間トレーの金属部材からは放電が観察された。この放電・加熱によりトレーの金属治具周辺にある糸束の中には透水量が０（ゼロ）であるものが見られ、明らかに性能不良の糸束が発生することが明らかとなった。

【００７０】

【表１】

	実施例1		実施例2		実施例3		実施例4	
	全糸束の平均値	最外性能のみ束の値	全糸束の平均値	最外性能のみ束の値	全糸束の平均値	最外性能の糸束の値	全糸束の平均値	最外性能のみ束の値
膜内径(μm)	195	195	200	200	195	195	195	195
膜外径(μm)	285	285	285	290	285	283	286	289
透水量(mL/(m²·hr·mmHg))	22	19	15	15	23	20	430	400
アルブミンの透過率(%)	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下	0.01以下
PVPの透過率(%)	4	4	4	4	5	5	72	72
膜内表面PVP量度(重量%)	35	35	30	30	44	44	36	36
水に不溶であるPVPの有無	有り	有り	有り	有り	有り	有り	有り	有り
溶出物試験液の吸光度	0.022	0.022	0.020	0.020	0.035	0.035	0.022	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し	無し	無し	無し	無し	無し	無し
血小板粘着量(LDH·Unit/m²)	15.6	15.7	17.7	17.5	4.1	4.1	14.0	14.1
血漿タンパク質吸着量(mg/g)	2.2	2.2	5.5	5.6	1.9	1.9	2.0	2.0
乾燥前膜圧潰膜の透水量(mL/m²·hr·mmHg)	190	190	170	170	260	260	3100	3100
乾燥前膜圧潰膜のアルブミンの透過率(%)	0.52	0.53	0.34	0.34	0.35	0.36	0.51	0.51
乾燥前膜圧潰膜のPVPの透過率(%)	77	77	84	84	84	84	99	99

【0071】

【表2】

	比較例1	比較例2	比較例3	比較例4	比較例5	比較例6
膜内径(μm)	195	201	200	196	202	190
膜外径(μm)	282	291	292	295	291	281
透水量(mL/(m²·hr·mmHg))	22	35	16	960	9	15
アルブミンの透過率(%)	0.01以下	0.01以下	0.01以下	0.37	0.01以下	0.01以下
PVPの透過率(%)	4	5	4	79	0	4
膜内表面PVP量度(重量%)	35	46	28	38	34	36
水に不溶であるPVPの有無	無し	有り	有り	有り	有り	有り
溶出物試験液の吸光度	0.047	0.035	0.016	0.020	0.020	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し	無し	無し	無し	無し
血小板粘着量(LDH·Unit/m²)	15.5	3.8	19.2	15.4	15.1	16.6
血漿タンパク質吸着量(mg/g)	2.1	2.1	6.9	2.8	2.1	3.0
乾燥前膜圧潰膜の透水量(mL/m²·hr·mmHg))	190	310	130	8500	76	190
乾燥前膜圧潰膜のアルブミンの透過率(%)	0.33	0.38	0.32	0.60	0.17	0.31
乾燥前膜圧潰膜のPVPの透過率(%)	77	85	76	100	52	76

【0072】

【表3】

	比較例7	
	全糸束の平均値	最外性能の糸束の値
膜内径(μm)	195	191
膜外径(μm)	255	230
透水量(mL/m²·hr·mmHg)	16	0
アルブミンの透過率（%）	0.01以下	測定不可能
PVPの透過率（%）	3	測定不可能
膜内表面PVP濃度(重量%)	35	35
水に不溶であるPVPの有無	有り	有り
溶出物試験液の吸光度	0.022	0.022
溶出物試験液中の膜孔保持剤の有無	無し	無し
血小板粘着量(LDH-Unit/m²)	15.0	測定不可能
血漿タンパク質吸着量（mg/g）	2.1	2.1
乾燥前親潤膜の透水量(mL/m²·hr·mmHg)	190	190
乾燥前親潤膜のアルブミンの透過率（%）	0.32	0.32
乾燥前親潤膜のPVPの透過率（%）	77	77

【００７３】

【発明の効果】本発明の乾燥装置によれば、糸束状に製束された湿潤膜をマイクロ波照射により複数束同時に乾燥する場合においても、一部の糸束に性能不良を生ずることなく中空糸膜を乾燥することができる。製造された中空糸膜は、膜からの溶出量が極めて少なく、血液タンパク質や血小板の付着が少ない優れた透析性能を有することから医薬用途、医療用途、及び一般工業用途に用いることができる。

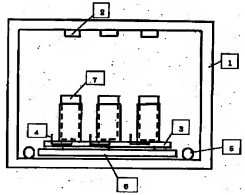
【図面の簡単な説明】

【図１】本発明の血液浄化膜の製造装置の一例を示す正面図である。

【符号の説明】

1　容器
2　マイクロ波照射手段
3　糸束を固定し搬入・搬出する手段
4　通風手段
5　液体通過手段
6　回転手段
7　糸束

【図１】



フロントページの続き

Fターム(参考) 3L113 AA03 AC12 BA01 CA08 DA24
4C077 AA05 BB01 GG20 LL05 NN03
PP02 PP03 PP13 PP15
4D006 GA13 MA01 MB06 MC40X
MC62X NA05 NA12 NA50
NA62 NA64 PB09 PB52